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RANDOMISED CLINICAL TRIAL TO COMPARE THE SEDATIVE EFFECTS OF ORAL TRICLOFOS WITH ORAL MIDAZOLAM AS PREMEDICANTS IN PAEDIATRIC PATIENTS

ABSTRACT:

Background: Surgery in paediatric patients is a stress to both parents and the children. The fear and anxiety originates mainly from the fear of needle pricks and separation of the children from their parents, to be taken away by strangers with mask and cap. So premedication to cause sedation and anxiolysis is a must.A prospective double blinded randomized clinical trial was conducted to compare oral triclofos and midazolam.

Aim of the study: The main objective is to compare the sedative effects of oral triclofos with oral midazolam when used as premedicants in paediatric patients for day care surgery. The study also focused on the drug acceptance, parental separation and mask acceptance at induction of anaesthesia.

Materials and methods: 150 children in the age group of 2-9 years, belonging to ASA 1 status were randomly assigned into two groups, Tand M with 75 children in each group and received Triclofos 75mg/kg and Midazolam 0.5mg/kg orally 45 minutes before surgery.The preoperative sedation scores were assessed at repeated intervals. The parent separation score was assessed at the shifting of the children

to the operation room. The mask acceptance score at induction of anaesthesia was also noted. The postoperative sedation score was assessed for the next 6 hours postoperatively and the difference in the two groups noted.

Results:

Triclofos was accepted better by the children than midazolam , produced higher sedation levels when given in the dose of 75mg/kg after 45 minutes of administration than midazolam 0.5mg/kg. Hemodynamic variables were comparable in the two groups. Though the parental separation score was comparable between the two groups, Triclofos provided good mask acceptance and postoperative recovery.

Conclusion:

Triclofos is a better and safe sedative premedicant than midazolam in paediatric patients.

Key words: Children, midazolam, premedication, sedation, triclofos.

RANDOMISED CLINICAL TRIAL TO COMPARE THE SEDATIVE EFFECTS OF ORAL TRICLOFOS AND ORAL MIDAZOLAM AS PREMEDICANTS IN CHILDREN

INTRODUCTION:

Surgery in paediatric age group is a great stress to both the parents and the children. The feeling of fear, anxiety and insecurity is mainly due to the separation of the child from the parent and also the encounter of strangers with mask and caps. Moreover children are also apprehensive of the needle prick and a mask that puts them in a state of doom. So to calm down the child and to obtain their co-operation during parent separation, a premedicant is necessary. Various forms of premedicant drugs are available like oral formulations, nasal spray, sublingual preparations, intramuscular injections, rectal suppositories etc. Out of these oral formulation is more easier and simpler to administer to children. Children are more compliant with the oral formulations which are usually prepared as flavored syrup making it acceptable by the children.

Out of the commonly used premedicant drugs, oral triclofos and oral midazolam are better sedatives and free of major adverse effects. So this study is conducted to study the sedative effects of both these drugs;

also the adverse effects and the anxiolytic effects will be compared. These drugs leave the child sedated and withdrawn from surroundings which allows a calm child entering the theatre instead of a crying and agitated child. These drugs also have the advantage of short duration of action so that the child can be discharged on the same day. So these drugs are being used predominantly in daycare surgeries.

Aim of the study:

To compare the sedative effects of oral triclofos and oral midazolam as a premedicant in children.

Secondary objective:

To compare the drug compliance, parent separation score and mask acceptance score of oral triclofos and oral midazolam.

PREMEDICATION IN CHILDREN:

Premedication is used in children not only to cause amnesia but also to allay the fear and anxiety from their minds. Parental separation in such a stressful situation like surgery makes them more restless and violent. The need for children to be in an unaccustomed place and situation, under the care of strangers during surgery is the main reason for all the hemodynamic responses and the psychological behavior disorders of the children. So premedication can be used to make them sleep and calm, make the child detached from the surroundings in a state of deep sleep which takes away the fear from the children. Preoperative anxiety causes unpleasant experience for the patient and also makes the induction and recovery from anaesthesia more complicated.

Premedication not only allays the anxieties about surgery, parent separation, the feel of pain, and about body disfigurement, but also allows a smoother and safer induction of anaesthesia.

Sedation can be defined as a state of drowsiness or sleep from which a subject can be aroused whereas anaesthesia is an unarousable state in which vital respiratory reflexes may be lost. So only conscious sedation is recommended as premedication. Using subanaesthetic doses

of anaesthetic drugs to cause sedation is not advisable. So non anaesthetic sedative drugs are preferred.

When selecting a premedication, three important factors which should be remembered are[4]:

1. A child's major fear about hospitalization is because of pain from needles and injections. For children, hospitalization is synonymous with needles. Children tend to remember the premedication injection more than the operative procedure pain. Thus any form other than intramuscular is preferred for premedication.
2. Children with frequent hospitalization need more preoperative medication than do the children coming for the first surgery. Experiences in the previous hospitalization forms the basis for their fears, so questions about the past experiences are invaluable. The previous anaesthetic record if available should be reviewed, with careful attention to the premedication agent used and its effects.
3. Premedication effects in children vary producing different effects with some children sedated,but some excited and restless. Few children may require about twice the recommended dose to produce desired level of sedation.

Some of the commonly used sedative drugs in children are as follows:

Opioids:

Not preferred in infants younger than 6 months. Premedication with opioid may cause unpleasant dysphoria and also preoperative and postoperative vomiting. Various routes of administration by which opioids can be given are oral, rectal, intravenous, intramuscular, and transmucosal routes. Intranasal and oral transmucosal forms of administration has been focused with interest in the recent years.

Fentanyl given in the dose of 0.5mcg/kg intravenously, 10 to 15 mcg/kg oral transmucosal.

Morphine 0.1-0.2 mg/kg intramuscular

Meperidine 1-2 mg/kg intramuscular

Sufentanil 1-3 mcg/kg intranasal

Benzodiazepines :

Midazolam is a water soluble benzodiazepine and has a rapid onset and a shorter duration of action. It is water soluble which is responsible for better absorption after intramuscular injection .Peak plasma concentration of Midazolam occurs 45 minutes after intramuscular injection, but the anxiolytic effects takes 5 to 60 minutes.

Its duration of action is usually 2 hours , ranging from 1 to 6hours.It has been approved and marketed as an oral preparation recently, and has become the most commonly administered premedication. Oral dose of midazolam is 0.25-0.75mg/kg. Intravenous preparation of midazolam can be given orally along with a vehicle like flavored syrup or fruit juices and has been proved effective in many studies[26] . Nasal midazolam is also reported to be highly effective in reducing anxiety in children by 10 to 12 minutes of administration but the disadvantage of nasal midazolam is irritation of the nasal passages. Midazolam is also administered sublingually (0.2 to 0.3 mg/kg) but difficult to prevent children from swallowing or spitting out immediately. Rectal dose of midazolam is 0.5 to 1 mg/kg.

Flunitrazepam can be given as a rectal premedication in doses of 0.04mg/kg. Triazolam reaches peak serum concentrations in 1 to 2 hours due to short half life; 0.02mg/kg orally is effective.

Diazepam has greater fat solubility and CNS effect than midazolam. Diazepam metabolized to desmethyldiazepam which is equally active pharmacologically like the parent compound. It is given in the oral dose of 0.3 to 0.5 mg/kg. It is not a preferred choice in children because of the immature liver function. Diazepam is less effective when

administered rectally than midazolam ; intramuscular administration is painful and causes irritation.

Barbiturates:

Only used rarely because of availability of short acting benzodiazipines. Methohexital has a relatively shorter half life, can be used rectally in the dose of 20 to 30 mg/kg and intramuscular in the dose of 10 mg/kg. This induces sedation in 15-20 minutes but has a unpredictable systemic absorption and possibility of hypersensitivity. Side effects are hiccups, apnea, airway obstruction, laryngospasm, seizures. Any rectal mucosal abnormality causes increased absorption of the drug leading to cardiac arrest. Methohexital is contraindicated in patients with porphyria, Temporal lobe Epilepsy and hypersensitivity. Barbiturates have the disadvantage of hyperalgesia which may cause agitation in children due to pain. Thiopentone can be given rectally in the dose 20 to 40 mg/kg.

Phencyclidine:

Ketamine is a phencyclidine derivative which blocks the NMDA receptor. Mechanism of action is by central dissociation of cortex from limbic system, providing analgesia and sedation but preserves the upper airway muscle tone and respiratory drive.It is a bronchial smooth muscle

relaxant and used in cases of bronchospasm. Since it increases secretions , an antisialogogue has to be administered along with it. Hallucinations may occur at the time of recovery which can be avoided by co-administration of a benzodiazepine. Ketamine is not only used for induction but also for maintenance of anaesthesia in children. Intramuscular , oral , nasal transmucosal and rectal routes used for administration. Oral ketamine can be given alone or combined with oral midazolam. Orally given as 3-6mg/kg, nasally 3mg/kg,rectally 6-10mg/kg and intramuscularly as 2-10 mg/kg.

Chloral hydrate and triclofos:

Chloral hydrate and triclofos induce sedation effectively when given orally. They are metabolised to trichlorethanol which cause drug residual effect and prolonged sedation. Chloral hydrate tastes unpleasant and also causes gastric irritation. Chloral hydrate contraindicated in patients with liver disease because the metabolism will be delayed which can lead to metabolic acidosis, renal failure and hypotonia. Airway obstruction and deaths have also been reported. Though triclofos is more palatable, it is slower to act and also less potent than chloral hydrate.

Contraindications for sedation are:

Abnormal airway

Raised intracranial pressure

Depressed conscious level

History of sleep apnoea

Respiratory failure

Cardiac failure

Neuromuscular disease

Bowel obstruction

Active respiratory tract infection

Known allergy or adverse reaction to sedative

Child too distressed despite adequate preparation

Older child with severe behavioural problems

Consent refusal by parent or patient.

SCORING SYSTEMS:

Various sedation scores are used worldwide . One internationally accepted score is Ramsay score:

Level	Characteristics
1	patient awake, anxious, agitated or restless
2	patient awake, co-operative, oriented and tranquil
3	patient drowsy, with response to commands
4	patient asleep, brisk response to glabella tap or loud auditory stimulus
5	patient asleep, sluggish response to stimulus
6	patient has no response to firm nail bed pressure or other noxious stimuli

This score was used in this study.

PARENTAL SEPARATION SCORE:

Though many scores for separation from parents available, this is more easy and practical.

1	Calm and sleepy
2	Apprehensive but withdrawn from surroundings
3	Crying
4	Agitated but difficult to control

This score was used in this study.

FACE MASK ACCEPTANCE SCORE:

Four point score:

1	Poor	Afraid, combative, crying
2	Fair	Moderate fear of mask, not easily calmed
3	Good	Slight fear of mask, easily calmed
4	Excellent	Unafraid, cooperative, accepts mask easily

The above score was used in the study.

Melatonin:

Induces natural sleep successfully when given in doses ranging from 2-10 mg orally.

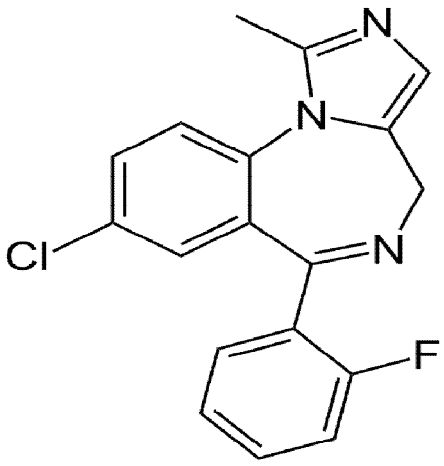
Alpha agonists:

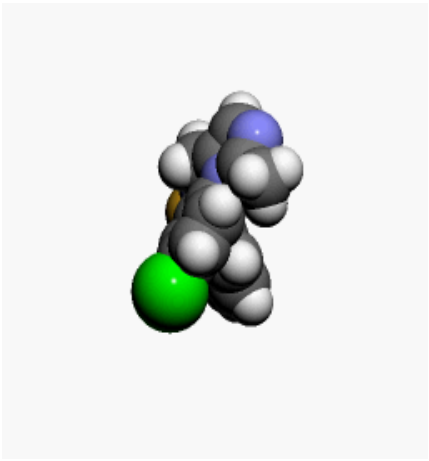
Oral clonidine premedication with 1 to 10 mcg/kg will produce a good sedation . Though oral clonidine possesses several desirable aspects for premedication , notably sedation and analgesia, the drug needs to be administered 60 minutes before induction, which is impractical . Peak plasma concentration of clonidine occurs between 60 to 90 minutes for oral formulation and 50minutes for rectal preparation. Newer drugs like alpha 2 agonists, have now emerged as alternatives for premedication .Dexmedetomidine a highly selective alpha 2 agonist has sedative and analgesic effects.It has limited effects on cardiorespiratory function.

PHARMACOLOGY

MIDAZOLAM:

STRUCTURE OF MIDAZOLAM:





Introduction:

Midazolam was developed by Hoffman-La-Roche in the 1970s.

Midazolam is a water soluble benzodiazepine. It has an imidazole ring

which contributes to the basicity, rapid metabolism and stability in aqueous solution. It has replaced diazepam as a premedicant. Midazolam is a good amnestic and twice as potent as diazepam. It is available as a closed and open structure which is pH dependent. It is available as a standard syrup preparation.

Chemical structure:

8-Chloro - 6-(2- fluorophenyl) -1- methyl -4H- imidazo(1,5-α)(1,4) benzodiazepine Hydrochloride

Physical properties:

The pK of midazolam is 6.5, which permits preparation of salts that are soluble in water. Injectable solution buffered to acidic pH of 3.5. This is significant because the structure of midazolam whether open ring or closed ring structure is dependent on the pH with the ring remaining open at pH < 4 , maintaining water solubility. The ring will close at pH >4, so exposure to physiological pH makes the drug highly lipid soluble . Basicity of the drug allows it to be mixed with salts like lactic acid, hydrochloric acid which is responsible for the water solubility.The hydrochloride solution is better tolerated when given intravenously or intramuscularly.

Water solubility obviates the need for a solubilising preparation such as propylene glycol which may interfere with absorption after intramuscular injection or may cause venoirritation when given intravenously. Midazolam is compatible with lactated Ringer solution and can be mixed with the acidic salts of other drugs including opioids and anticholinergics.

Mechanism of action:

Midazolam acts by facilitating the effects of gamma-aminobutyric acid which is the inhibitory neurotransmitter of the central nervous system. It increases the affinity of the receptors for GABA instead of stimulating them resulting in enhanced chloride gating channels opening causing increased chloride conductance and produces hyperpolarisation of the postsynaptic cell membrane. There is resistance to excitation of the post synaptic neurons which is responsible for anxiolysis, sedation, anterograde amnesia and anti-convulsant effect.

Pharmacokinetics:

Midazolam undergoes rapid absorption from the gastrointestinal tract and passes promptly across the blood brain barrier, but has a slow effect site equilibration time. So intravenous doses should be spaced before a repeat dose is to be administered. Only about 50% of the orally

given drug is \available in the systemic circulation because of a substantial first pass effect.

Midazolam is extensively plasma protein bound.The lipid solubility of midazolam leads to rapid redistribution from the brain to other inactive tissue sites because of which it is short acting. The elimination half-time is usually 1 to 4 hours; but it may get doubled in geriatric patients which reflects age related decreases in hepatic blood flow.

Metabolism:

Midazolam is rapidly metabolized by cytochrome P-450 enzymes of the liver and small intestine to both active and also inactive metabolites. The principal metabolite is 1-hydroxymidazolam; has approximately half the activity of the parent compound. This metabolite is conjugated to 1-hydroxymidazolam glucuronide and subsequently cleared by the kidneys. The glucuronide metabolite has substantial pharmacologic activity when present in high concentrations which may occur in critically ill patients with renal insufficiency receiving continuous intravenous infusions.

EFFECTS ON VARIOUS SYSTEMS:

CENTRAL NERVOUS SYSTEM:

Midazolam causes a reduced cerebral metabolic oxygen requirements and decreases cerebral blood flow. Cerebral vasomotor response to carbondioxide is preserved. Midazolam is a potent anticonvulsant effective in treatment of status epileptics. Parodoxical excitement occurs in <1%.

RESPIRATORY SYSTEM:

Midazolam produces dose dependent decrease in ventilation. When administered rapidly in large doses, that too with an opioid, transient apnea may occur .Also depresses the reflex of swallowing and decrease upper airway activity.

CARDIOVASCULAR SYSTEM:

Midazolam produces a decrease in systemic blood pressure and increase in heart rate. Cardiac output is not altered by midazolam. It does not prevent blood pressure and heart rate responses evoked by intubation of the trachea.

CLINICAL USES:[3]

Midazolam is the most widely used benzodiazepine for pre medication in paediatric patients, intravenous sedation, and induction of anaesthesia.

PREOPERATIVE MEDICATION:

Midazolam is the most often used oral preoperative medication for Children. Oral midazolam syrup (2mg/ml) when given at a dose of 0.5 mg/kg is effective for producing sedation and anxiolysis with minimal effects on ventilation. When 0.5mg/kg is administered orally 30 minutes before induction of anaesthesia , there is reliable sedation and anxiolysis in children, that too without producing delayed awakening .

INTRAVENOUS SEDATION:

Midazolam when given intravenously for sedation is effective during regional anaesthesia as well as for brief therapeutic procedures. Reduced hypoxic drive can lead to depressed ventilation and it is the most significant side effect of midazolam which is exaggerated when used along with opioids and other CNS depressant drugs.

INDUCTION OF ANAESTHESIA:

Anaesthesia can be induced by the dose of 0.1 to 0.2 mg/kg iv, over 30 to 60 seconds which is facilitated by a small dose of opioid .

MAINTENANCE OF ANAESTHESIA:

Midazolam may be administered to supplement opioids , propofol and /or inhaled anaesthetics during maintenance of anaesthesia.

POSTOPERATIVE SEDATION:

Long term intravenous midazolam used for sedation in intubated patients usually results in relative saturation of the peripheral tissues with midazolam and clearance from the systemic circulation becomes less dependent on redistribution into peripheral tissues and more dependent on hepatic metabolism. Pharmacologically active metabolites may accumulate with prolonged IV administration.

CONTRAINDICATIONS:

Hypersensitivity, acute narrow angle glaucoma, shock, hypotension or head injury. Kidney or liver disease may slow down the elimination leading to prolonged duration of action and exaggerated effects.

SIDE EFFECTS:

1. Long term use is associated with deficits in memory.

2. Depression may be worsened.

3. With intravenous injections, paradoxical excitement can occur causing anxiety, involuntary movements, aggressive or violent behavior, uncontrollable crying or verbalization.

4. Sleepiness and impaired psychomotor and cognitive functions may persist next day as hangover effects.

5. Respiratory depression hypotension and increased heart rate.

TOLERANCE AND WITHDRAWAL:

Use for more than 4 weeks may result in dependence, tolerance and withdrawal if stopped abruptly.Withdrawal symptoms can range from insomnia and anxiety to seizure and psychosis. Tolerance and the resultant withdrawal syndrome are due to the receptor down regulation and $GABA_A$ receptor expression alteration. These effects can be minimized by gradual reduction of dose of midazolam.

OVERDOSE:

Symptoms of midazolam overdose include ataxia, dysarthria, nystagmus, slurred speech, somnolence, mental confusion, hypotension, respiratory arrest vasomotor collapse,impaired motor functions,impaired coordination, impaired balance, dizziness,coma and death.

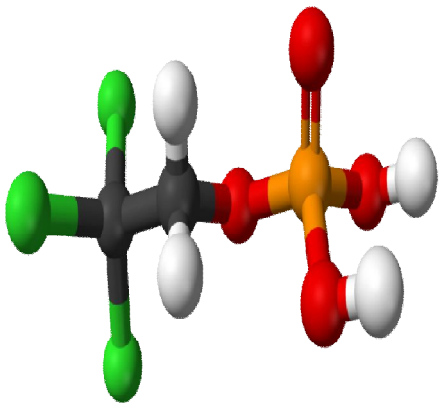
TREATMENT OF OVERDOSE:

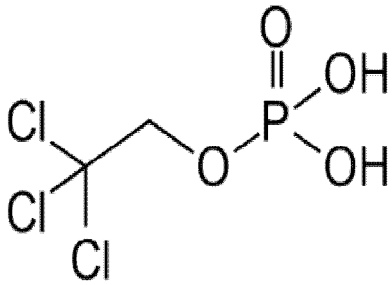
Flumazenil is a specific benzodiazepine antagonist which is given in the dose of 0.01-0.02 mg/kg. Repeat dose is given every 1 minute. The onset of action occurs in 1 to 2 minutes and its effects last for 30-60 minutes.

Opioids and other sedatives are not antagonized. Prolonged observation is necessary as resedation can occur in 1 hour. Flumazenil should not be used for routine dose reversal. Children may have exacerbations with Flumazenil.

TRICLOFOS

STRUCTURE OF TRICLOFOS





CHEMICAL STRUCTURE:

2,2,2-trichloroethanol dihydrogen phosphate $C_2H_4Cl_3O_4P$

INTRODUCTION:

Triclofos is a chloral sedative which is non barbiturate sedating drug which potentiates the central nervous system depression. It is a hypnotic drug which is used in disabling sleeplessness.It is always used as a second line drug in insomnia.Triclofos, being a prodrug is usually metabolized in the liver to trichloroethanol . It is long acting and may

cause sedation the next day also due to the slow action. It does not possess analgesic property.

MECHANISM OF ACTION:

Triclofos after being converted to trichloroethanol acts on the brain to cause sleep by shortening the time taken to fall asleep. There are no specific receptors on which triclofos acts.

CLINICAL USES:

Triclofos is used as a sedative for short procedures like dental procedures , used as premedication before major surgeries in paediatric age group. Triclofos is more palatable than its congener chloral hydrate and readily accepted by children due to its sweet taste which is available as oral syrup. The dose is 50-75mg/kg orally.

ONSET OF ACTION: 30-40 MINUTES

DURATION OF ACTION: 6-8 HOURS

CONTRAINDICATIONS:

- Marked hepatic or renal impairment
- Cardiac diseases
- Patients with gastritis
- Allergy to chloral hydrate

- Pregnancy
- Breastfeeding

SIDE EFFECTS:

Cardiac arrhythmias, Jaundice, Albuminuria, Abdominal distension, Headache, Ataxia, Skin rashes, Confusion, Hallucination, Gastric irritation, Light headedness, Nightmares, Nausea, Vomiting, Diarrhoea, Constipation, Delirium, Flatulence, Dizziness, Dependence.

DRUG INTERACTIONS:

Alcohol, Antipsychotics, eg chlorpromazine, haloperidol , Baclofen, Barbiturates, eg phenobarbital, amobarbital , Benzodiazepines, eg diazepam, temazepam , MAOI antidepressants , Other sedatives eg zopiclone ,Sedating antihistamines such as chlorpheniramine, hydroxyzine, promethazine, Opioid analgesics like morphine, codeine, Tricyclic and related antidepressants like amitriptyline, maprotiline.

PRECAUTIONS:

Triclofos should be used only for short term as it may cause dependence. It should be used with caution in elderly patients and in patients with alcohol or drug abuse. It may be used in patients with personality disorders with caution.

REVIEW OF LITERATURE

1. Aruna Parameswari, et al[2], in journal of anaesthesiology clinical pharmacology 2010;26(3) 340-344, had published a study "Sedative and anxiolytic effects of midazolam and triclofos oral premedication in children undergoing elective surgery: A comparison". The aim of the study was to compare the efficacy of oral midazolam and oral triclofos as premedicants in children producing sedation, anxiolysis and acceptance of face mask. Forty children, ASA I, aged between 1 and 10 years posted for elective surgery were included in the study. As premedication, Group 1 patients were given oral midazolam 0.5mg/ kg, and Group 2 patients were given 75mg/ kg of oral triclofos. The acceptance of premedication, level of sedation, level of anxiolysis and acceptance of face mask was assessed.In Group 1, 80% patients were awake, but calm, 5% patient were asleep during the assessment done 30 minutes after drug administration, while in Group 2, only 10% patients were awake and calm, 65% patients of the patients were asleep (p value 0.000). In Group I, 50% patients never resisted the face mask and 40% patients had slight resistance whereas Group 2, 10% patients had no resistance to face mask and 55% patients had slight resistance. Face mask acceptance was better in Group 1 (p value of 0.014).

The author concluded that oral triclofos when given in the dose of 75mg/kg produces better sedation and anxiolysis compared to oral midazolam 0.5mg/kg, but acceptance of face mask was better with midazolam. The limitations of triclofos were the longer time for the onset of action , peak effect and also the drowsiness it produces.

2.JULIET D. BOYD AND MARGARET L. M. MANFORD[6], in a study on "PREMEDICATION IN CHILDREN A Controlled Clinical Trial of Oral triclofos and Diazepam" in the British journal of anaesthesia May 1973, 45, 501-506, tried to compare a hypnotic triclofos with a tranquiliser diazepam for premedication in children before minor ENT procedures. Children aged 2-9 years were included in the trial. Two matching syrups were made to contain optimum doses of diazepam and triclofos and labelled A and B and allocated on a random basis. The code remained in a sealed envdope until the trial completion and the results analysed. The constitution of the syrups was such that a child received either 0.2 mg/kg of diazepam or 71 mg/kg of triclofos, 2 hours before induction of anaesthesia. atropine sulphate 0.03 mg/kg was added to the syrup. The children were monitored preoperatively and postoperatively. Children asleep or drowsy were given an inhalation induction and those awake given an intravenous injection. Post- operative analgesia provided by intramuscular injection of dihydrocodeine tartrate 1-1.25 mg/kg.*It*

concluded that triclofos was better than diazepam in suppressing the salivary secretions and general behavior in the procedure room.

3.**Sujata chaudhry**, et al[1], in journal of anaesthesiology clinical pharmacology jan-march 2014,volume 30, issue 1 53-58, did a study named "Is midazolam superior to triclofos and hydroxyzine as premedicant in children?" The study was done to compare the efficacy of the drugs midazolam, triclofos and hydroxyzine when used as premedication in children who are undergoing lower abdominal surgeries.

Sixty ASA PS I or II patients, who are in the age group 2-8 years , scheduled for elective lower abdominal surgery were included in thestudy. The patients randomly divided into 3 groups M, T and H of 20 children each and received midazolam 0.5 mg/kg, triclofos 75 mg/kg and hydroxyzine 0.5 mg/kg respectively, orally 60 min before surgery. The drug acceptability, sedation level, anxiety levels during parent separation and on face mask application were assessed.

The acceptance of the drugs midazolam and hydroxyzine were found to be better than triclofos. Hydroxyzine produced lesser sedative effect as compared to both midazolam and triclofos without major adverse effects. It was concluded in the study that midazolam is a better

premedicant when the sedation, anxiolysis and safety are compared to that of triclofos or hydroxyzine .Triclofos proved as an acceptable alternative whereas hydroxyzine was not proved as a good premedicant according to this study.

4. L. SAARNIVAARA, et al[17], in a study published in British journal of anaesthesia 1988 (61) 390-396, "COMPARISON OF CHLORAL HYDRATE AND MIDAZOLAM BY MOUTH AS PREMEDICANTS IN CHILDREN UNDERGOING OTOLARYNGOLOGICAL SURGERY" gave Chloral hydrate in the doses of 25, 50 or 75 mg /kg or midazolam 0.4, 0.5 or 0.6 mg/ kg, orally in combination with atropine 0.03 mg /kg, to 248 children. Chloral hydrate though was less palatable than midazolam, the anxiolytic effect in the dose 75 mg/ kg was good in children < 5 yr, whereas the other two doses of chloral hydrate, and all the doses of midazolam, had provided only fair anxiolysis. In older children ,all doses of both the premedicants proved as good anxiolytics. The antisialagogue effect was satisfactory in 83-90% of each group. Restlessness was observed 20 min after extubation, in 15-25% of the younger children premedicated with chloral hydrate 25 mg/ kg or with midazolam 0.4 or 0.6mg/kg. The study concluded that midazolam should be given at a dose of 0.5 mg/kg in children younger <5 years and

0.4-0.5 mg/kg for older children and that chloral hydrate is not recommended as it is bitter to taste and unpalatable for children.

5.Shabbir A, et al,[8] published a study on "Comparison of oral midazolam and triclofos for conscious sedation of uncooperative children" in the journal of clinical paediatric dentistry 2011, volume 36, number 2 189-196. The aim of the study was to compare the safety and efficacy of two orally administered sedative drugs triclofos 70 mg/kg and midazolam 0.5 mg/kg in paediatric dental patients. The conclusion was oral midazolam when used in a dose of 0.5 mg/kg is more effective than triclofos in regulating the behavior of children during the procedure.

6.Bhatnagar S, et al[20], in JOURNAL OF INDIAN SOCIETY OF PEDODONTICS AND PREVENTIVE DENTISTRY, Apr - Jun 2012 , Issue 2 , Vol 30 109-114 , had published a study on "Comparison of oral midazolam with oral tramadol, triclofos and zolpidem in the sedation of pediatric dental patients: An in vivo study". The aim of the study was to compare the effects of oral midazolam with oral tramadol,oral triclofos and oral zolpidem to produce conscious sedation in paediatric patients coming for dental procedures. 60 children who reported to the department, who were anxious and fearful ,were given conscious sedation for the accomplishment of dental treatment.They were randomly assigned

to four groups. Statistical analysis done using Kruskal Wallis Test and decision criterion was to reject the null hypothesis if the P -value < 0.05. The observation was that there was a statistical significant difference in median scores for the level of sedation between the different groups (P < 0.001).

The study concluded that midazolam 0.5mg/kg is the most effective drug for conscious sedation in paediatric dental patients. Tramadol 2mg/kg gave results equivalent to midazolam and triclofos 70mg/kg though had good results during the procedure, the effect was not comparable with midazolam. Zolpidem though a good hypnotic did not produce the expected level of sedation.

7.Razieh Fallah, et al[14], in a study "Oral Chloral Hydrate *vs.* Intranasal Midazolam for Sedation During Computerized Tomography" published in the Indian Paediatrics, 2013, 50, 233-235, aimed to compare the efficacy and safety of oral chloral hydrate with intranasal midazolam when used as sedative in paediatric age group for performing computerized tomography of brain. *They concluded that oral chloral hydrate is more effective than intranasal midazolam in sedating the uncooperative children presenting for CT scan of the brain.*

8. **Singh N, et al,**[24] in a study in the Journal of Clinical Pediatric Dentistry 2002 Winter;26(2),161-164, "A comparative evaluation of oral midazolam with other sedatives as premedication in pediatric dentistry" evaluated the efficacy and safety of oral midazolam as a sedative compared with other older agents like triclofos and promethazine in paediatric dentistry. The study was conducted on ninety children in the age group of 3-9 years of ASA 1 requiring some short dental procedure. The patients were randomized into three study groups, on the basis of the drugs to be administered. After administration of drugs, the effects were evaluated in terms of onset of action, sedative effect, ease of treatment completion, recovery time and postoperative amnesia. *The study concluded that oral midazolam is the best drug out of all the three as a sedative in terms of safety, efficacy, recovery and postoperative amnesia.*

9. **ARATHI PAPINENI, et al,**[15] in International journal of Paediatric dentistry 2014, 24, 2-14, published a study on "Safety of oral midazolam sedation use in paediatric dentistry: a review". The study aimed at evaluating the side effects and other adverse outcomes when oral midazolam was used for behavior management in paediatric dentistry. A review of published literature relating to the safety and side effects of oral midazolam used in paediatric dental procedures was done. Both randomized controlled trials and non-randomised studies were

assessed. The side effects reported were recorded and classified as either significant or not. The percentage prevalence of significant or minor side effects per episode of treatment was calculated. Sixteen papers in the randomised controlled trials met the inclusion criteria.The side effects recorded were not considered as significant. Minor side effects were reported (14%), with nausea and vomiting being the most frequently recorded (6%). 11 papers of non-randomised studies were also included. No significant side effects recorded.Minor side effects were recorded (8%), with paradoxical reaction being the most common at 3.8%. *The author concluded that significant and major side effects were rare and minor events may occur, but the precise figure of it could not be achieved due to a poor reporting of such events.*

10.K. E. Wilson,et al,[16] in British dental journal, April 2002, volume 192, no 8, 457-462, published "A study of the effectiveness of oral midazolam sedation for orthodontic extraction of permanent teeth in children: a prospective, randomised, controlled, crossover trial". The aim of the study was to assess the effectiveness , safety and acceptability of oral midazolam as a sedative when used for orthodontic extraction of permanent teeth in children. 26 children of age 10 – 16 years (ASA I), referred for orthodontic extraction of premolar or canine teeth under sedation, were included in the study. Each child had two treatment

sessions for the extraction of equivalent teeth on opposite sides of the mouth. Each subject was sedated with either oral midazolam (0.5 mg/kg) or nitrous oxide and oxygen (30%/70%) at first visit and the alternative form at second visit. At each visit two teeth were extracted, one upper and one lower. Heart rate, arterial oxygen saturation, respiration rate, sedation and behavioural scores were recorded every five minutes. Overall behaviour, patient acceptance and patient satisfaction were recorded at the end of treatment. Out of the 26 children in the study 12 were males and 14 were females. The mean age was 12.5 years. The mean heart rate and respiratory rate in both groups were similar, within acceptable clinical limits. The lowest mean arterial oxygen saturation levels for nitrous oxide and midazolam sedation were 97.7% and 95.0% respectively. Though midazolam had caused a greater oxygen desaturation, the range was within safe limits for conscious sedation. The mean sedation level was greater in the midazolam group compared with the nitrous oxide group . 88% of patients were prepared to have oral midazolam sedation again and 65% actually preferred oral midazolam to nitrous oxide sedation. *The study concluded that oral midazolam in the dose of 0.5 mg/kg appeared to be safe and effective form of sedation in children in the paediatric age group coming for dental procedures.*

11.Saad A Sheta, et al,[36] in the International journal of paediatrics 2009, compared different doses of oral midazolam for premedication in paediatric age group. The doses of 0.5mg/kg,0.75mg/kg and 1mg/kg were observed for effectiveness in anxiolysis during parental separation and venepuncture and *found that 0.75mg/kg oral midazolam as effective and acceptable dose as premedication and does not alter recovery time after general anaesthesia.*

12.Thomas R Vetter[38]**,** in the journal of clinical anaesthesiology, January-february 1993,volume 5, issue 1,58-61, by a study " A comparison of midazolam, diazepam and placebo as oral premedicants in younger children" *concluded that neither midazolam nor diazepam is necessary in children < 6 years and the routine use of premedication is not necessary in this age group. Premedication should be given based on the selective children at risk and with psychological imbalances.*

13**.Luz María Gómez B**[12] , et al, in Colombian journal of anaesthesiology 2013 41(1) 4-9 have published a study on " Efficacy of anesthetic premedication in pediatric patients using oral midazolam and acetaminophen. Observational study". A prospective descriptive observational study was conducted to analyse the efficacy of the premedication with a mix of midazolam and acetaminophen, sedation – anxiety scores were given and the parent separation score and mask

acceptance score were analysed. 216 children ASA PS I or II, scheduled for procedures that required general anesthesia. Anxiety-sedation scales (modified Yale scale and RASS), and tolerance to parent separation were assessed.

The RASS scale showed that 92% of the patients were at an adequate sedation level to tolerate the facemask induction, while 86% of patients tolerated the separation from their parents. *This study concluded that midazolam and acetaminophen proved effective as premedication in children and reduced the anxiety in children at the time of parent separation and also acceptance of the inhalation anaesthetic induction in a better way, thus improving the whole experience both for the children as well as the parents.*

14.Chandni Sinha,[13] et al, in journal of anaesthesiology clinical pharmacology had published a study on "Comparative evaluation of midazolam and butarphanol as oral premedication in paediatric patients". The aim of the study was to compare the efficacy of oral midazolam in the dose of 0.5 mg/kg with oral butarphanol in the dose of 0.2mg/kg with regards to sedation, anxiolysis, rescue analgesic requirement and recovery profile. In this double blinded study, 60 pediatric patients of ASA class I and II inthe age group of 2–12 years posted for elective surgery were randomized to receive either oral midazolam (group I) or oral

butorphanol (group II) 30 min before induction of anesthesia. The children evaluated for levels of sedation and anxiety at the time of parent separation , venepuncture, and at facemask application for induction of anesthesia. Rescue analgesic requirement, postoperative recovery, and complications were also recorded. Butorphanol showed better sedation level than oral midazolam but the anxiolysis at parent separation of children were comparable. Midazolam was a better anxiolytic during venepuncture and on facemask application. Butorphanol reduces the need for supplemental analgesics perioperatively without increase in the side effects. *The author had concluded that Butorphanol had better sedation levels than oral midazolam but had comparable anxiolysis at separation of children from parent and also proved that midazolam as a better anxiolytic on venepuncture and facemask application. Butorphanol demonstrated additional analgesic property and reduced the need for supplemental analgesics without increase in side effects.*

15. Mohamed A Daabiss and Mohamed Hashish ,[9] published a study in the British journal of medical practitioners December 2011, volume 4, number 4, named "Dexmedetomidine versus ketamine combined with midazolam: a comparison of anxiolytic and sedative premedication ". The aim of the study is to evaluate the efficacy of oral dexmedetomidine as a hypnotic and anxiolytic when compared with oral ketamine and midazolam for paediatric premedication. 66 children posted

for elective surgical procedure were randomized into two groups, one group given dexmedetomidine 3mcg/kg and other group given 0.25 mg/kg of oral midazolam with 2.5 mg/kg of ketamine. Drug acceptance score was recorded. Hemodynamic variables, sedation score and anxiolytic score recorded before sedation and then every 5 minutes post drug administration upto next 30 minutes.Parent separation score and mask acceptance score recorded at 30 minutes and results noted. *The study concluded that premedication with midazolam/ketamine was superior to dexmedetomidine providing haemodynamic stability and good parental acceptance although dexmedetomidine was accepted by the children. No significant side effects in both the medications and emergence from anaesthesia is comparable in both the groups.*

16. NICOLE ALMENRADER,et al,[7] in Pediatric Anesthesia 2007, 17, 1143–1149, in the study "Premedication in children: a comparison of oral midazolam and oral clonidine" aimed at comparing the clinical effects of midazolam and clonidine.64 children were randomly assigned to receive either oral midazolam 0.5 mg/kg or oral clonidine 4 mcg/kg prior to mask induction. Drug acceptance, preoperative sedation and anxiolysis, quality of mask acceptance, recovery profile and parental satisfaction evaluated. The taste of oral clonidine judged as significantly better; 14% children rejected oral midazolam. Onset of sedation significantly faster after premedication

with midazolam (30 ± 13.1 min) than with clonidine (38.5 ± 14.6 min), but level of sedation significantly better after clonidine. Quality of mask induction equally successful in both the groups.A trend towards an increased incidence of emergence agitation after midazolam premedication was noted . Parental satisfaction significantly higher in Clonidine group. *The authors came to the conclusion that oral clonidine is superior to oral midazolam as a premedicant, mask acceptance comparable between both the groups but oral clonidine was better accepted by the children, had good sedation and smooth recovery and also better parent satisfaction.*

17. Ashu Mathai, et al,[11] in Anaesthesia: Essays and researches January-june 2011, 5(1), 67-71, published the study "Preanesthetic sedation of preschool children: comparison of intranasal midazolam versus oral promethazine" which aimed to analyse the efficacy of intranasal midazolam and orally administered promethazine in preanaesthetic sedative and calming effects in preschool children. Hundred preschool children undergoing elective surgery selected and sedated with either intranasal midazolam or oral promethazine syrup in the preoperative period. Levels of sedation till the period of mask placement for induction of general anesthesia was recorded. The two groups had comparable heart rates, respiratory rates, sedation scores, and emotional scores at all points of assessment (P>0.05). But, intranasal

midazolam had a significantly shorter onset of sedation as well as time to reach maximal sedation (P<0.001). *The conclusion of the study was that intranasal midazolam was equivalent to oral promethazine as a sedative and anxiolytic in preschool children undergoing surgery and that both the drugs are relatively easy to administer and do not require any additional equipment. The rapid onset and shorter duration to maximal sedation of intranasal midazolam makes the drug useful, particularly in the outpatient setting.*

18. Fazi L, et al,[25] published a study in Anaesthesia-Analgesia , 2001 January;92(1):56-61, "A comparison of oral clonidine and oral midazolam as preanesthetic medications in the pediatric tonsillectomy patient" comparing the effects of oral clonidine 4 mcg/kg and oral midazolam 0.5 mg/kg on the preanaesthetic sedation and postoperative recovery profile during tonsillectomy in paediatric patients with or without adenoidectomy.In this double-blinded study design, 134 ASA PS I-II children aged 4-12 yr randomized to receive a combination of either clonidine and placebo or placebo and midazolam at 60-90 min and 30 min, respectively,before the induction of anesthesia. Clonidine group children exhibited more intense anxiety on separation and during induction of anesthesia through a mask, measured by the modified Yale Preoperative Anxiety Scores and also had significantly lower mean intraoperative arterial blood pressures, shorter surgery, anesthesia, and

emergence times, and a decreased need for supplemental oxygen during recovery compared with the midazolam group. However, the clonidine group had larger postoperative opioid requirements, maximum excitement and pain scores. No differences between the two groups in the times to discharge readiness, postoperative emesis, unanticipated hospital admission rates, postdischarge maximum pain scores, and 24 h analgesic requirementsd were noted. The percentage of parents completely satisfied with the child's preoperative experience was significantly higher in the midazolam group but no differences in parental satisfaction with the recovery period. The results were that under the conditions of this study, oral midazolam is superior to oral clonidine as a preanesthetic medication in this patient population.When comparing oral clonidine (4 microg/kg) and midazolam (0.5 mg/kg) in children during tonsillectomy, clonidine group had greater preoperative anxiety and shorter surgery and anesthesia times, but required more postoperative analgesia whereas delayed recovery and discharge times did not differ. *The study concluded that midazolam is superior to clonidine for premedication in paediatric tonsillectomy.*

AIM OF THE STUDY :

To compare the sedative effects of oral triclofos with oral midazolam as a premedicant in paediatric patients for day care surgeries.

PRIMARY OBJECTIVE:

To compare the efficacy and safety of sedative effects of oral triclofos with oral midazolam as a premedication for the day care surgeries done under general anaesthesia in the paediatric patients.

SECONDARY OBJECTIVE:

To compare the drug compliance, parent separation score and the mask acceptance score of oral triclofos and oral midazolam.

MATERIALS AND METHODOLOGY:

Study design:

This is a prospective double blinded randomized clinical trial done in the Paediatric surgery theatre in Stanley medical college after getting approval from the institutional ethical committee. A sample size of 150 patients belonging to ASA PS 1 were randomly assigned into two groups namely Group M and Group T.

Patients undergoing elective day care surgeries were enrolled in the study. Randomization was done by draw of lots method. Midazolam and triclofos written on equal number of lots, 75 lots each. When the patient meets the criteria for study, the patient was asked to pick up a lot and the drug in the lot was given by the assistant professor of the theatre, who was not included the study. In the midazolam group, intravenous ampoule preparation of preservative midazolam containing 5mg/ml was mixed with flavored paracetamol syrup to make a volume of 0.5 ml/kg of that particular patient.The assistant professor maintained a list of the names of the patient, and the group to which they belong to.

PATIENT SELECTION :

150 patients of ASA I of both sex undergoing day care surgeries under general anesthesia. Sample size was 150 and was calculated with G*power 3.13 version with reference to parent study.

Analysis:

Input:

Tail(s) = Two

Effect size d = 0.5484637

α err prob = 0.05 Power

(1-β err prob) = 0.90

Allocation ratio N2/N1 = 1

Output:

Noncentrality parameter δ = 3.2678496

Critical t = 1.9770537

Df = 140

Sample size group 1 = 71

Sample size group 2 = 71

Total sample size = 142

Actual power = 0.9006717

INCLUSION CRITERIA :

ASA grade I

Age 2 to 9 years

Both Sex

Undergoing General Anesthesia

Undergoing day care surgeries

Children weighing less than or equal to 20 kg

EXCLUSION CRITERIA :

- Clinically significant cardiovascular, neurologic, renal, hepatocellular or gastrointestinal diseases.
- Patients with gastrointestinal disorder that affects the absorption of oral drug.
- Allergy to the drugs studied.

GROUPS :

Group M : patients receiving midazolam 0.5mg/kg (IV Midazolam containing 5mg/ml was mixed with flavored paracetamol syrup made to a total volume of 0.5 ml/kg)

Group T : patients receiving oral triclofos 75mg/kg (each ml containing 100mg made to a volume of 0.5 ml/kg)

MONITORING :

HR

SpO2

RR

SEDATION SCORE

MATERIALS :

- Commercially available oral triclofos syrup containing 100mg/ml
- Prepared oral midazolam formulation prepared by mixing 0.5 mg/kg of midazolam taken from a preservative free midazolam ampoule 5mg/ml in which was added to flavored paracetamol syrup.
- Drug filler
- Syringe
- 22G intravenous cannula and IV Fluids
- Drug for Caudal anaesthesia, 0.25% bupivacaine
- Drug Inj atropine and Inj Fentanyl
- All emergency drugs

METHODOLOGY :

150 patients with the average age of 2 –9 years undergoing day care surgeries under general anesthesia were randomized into two groups of 75 each by draw of lots method. A complete pre anaesthetic evaluation was done and the parents were explained about the effects, possible risks and complications of the premedicants in detail and informed consent was obtained.

The child was shifted to the premedication room and oral Midazolam 0.5 mg/kg(iv drug containing 5mg/ml made into total volume of 0.5 ml/kg mixed with flavored paracetamol syrup) or oral Triclofos 75mg/kg(each ml containing 100mg made to a volume of 0.5 ml/kg) was administered using a drug filler according to which group the child belongs to, by the assistant professor who was not involved in the study. Drug compliance scoring was done.

DRUG COMPLIANCE SCORE:

1	Good	Readily takes medicine
2	Fair	Accepts medicine with persuasion
3	Poor	Unwilling to take medicine or spits it out
4	Very poor	Refuses medicine

The level of sedation was assessed using the sedation score after 10 minutes, 20 minutes, 30 minutes and 45 minutes of drug administration.

RAMSAY SEDATION SCORE

Level	Characteristics
1	patient awake, anxious, agitated or restless
2	patient awake, co-operative, oriented and tranquil
3	patient drowsy, with response to commands
4	patient asleep, brisk response to glabella tap or loud auditory stimulus
5	patient asleep, sluggish response to stimulus
6	patient has no response to firm nail bed pressure or other noxious stimuli

The child was repeatedly assessed for the level of sedation and was sent to operation theatre after 45 minutes of oral administration of premedicant. While shifting the child to the operating room, parent separation score was assessed.

PARENT SEPARATION SCORE:

1	Calm and sleepy
2	Apprehensive but withdrawn from surroundings
3	Crying
4	Agitated but difficult to control

On arrival in the operation room, the patients' baseline heart rate , SPO2, RR were recorded. Patients monitored with pulse oximetry , ECG and heart rate.

Mask acceptance score was done in the operation room

MASK ACCEPTANCE SCORE:

1	Poor	Afraid, combative, crying
2	Fair	Moderate fear of mask, not easily calmed
3	Good	Slight fear of mask, easily calmed
4	Excellent	Unafraid, cooperative, accepts mask easily

Child was induced with sevoflurane 8% with O_2/N_2O mixture at 4 litres of fresh gas flow at 50:50 ratio of O_2 / N_2O.

Inj atropine 0.02mg iv in combination with Inj fentanyl 1 to 2mcg/kg given intravenously. When the child was breathing smooth and regular, and when there was centrally fixed eye gaze, sevoflurane dial settings stepped down to 2%.

Anesthesia was maintained with sevoflurane 2% and caudal block given using 0.25% of bupivacaine 1ml/kg. Intra –operative HR ,SPO2 , and RR are recorded every 5 min for first 30 min and subsequently every 10 min intervals till the end of surgery. Bradycardia (HR < 60) persisting for > 2 min if occured, was to be treated with Inj .Atropine 0.02 mg/kg IV boluses. Volatiles were discontinued at the end of Procedure. Ondansetron 0.2 mg/kg IV was given only if post operative nausea vomiting present. Sedation score, HR , SPO2 and RR were observed for next 6 hours.

Statistical analysis: The datas collected from the study, were statistically analysed.

The collected data was analysed with SPSS 16.0 version. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and S.D were used.

To find the significance difference between the bivariate samples in Paired groups Wilcoxon signed rank test was used for skewed data and paired sample t-test for the normal data & for Independent groups (Triclofos & Midazolam) Mann-Whitney U test for skewed data and unpaired sample t-test for the normal data was used.

For the multivariate analysis in the repeated measures the Friedman test was used. To find the significance in categorical data Chi-Square test was used. In all the above statistical tools the probability value .05 is considered as significant level.

OBSERVATION AND RESULTS:

P-Value	Highly Significant at P ≤ .01

P-Value	Significant at P ≤ .05

P-value	Not Significant at P > .05

DEMOGRAPHIC VARIABLES

GENDER DISTRIBUTION:

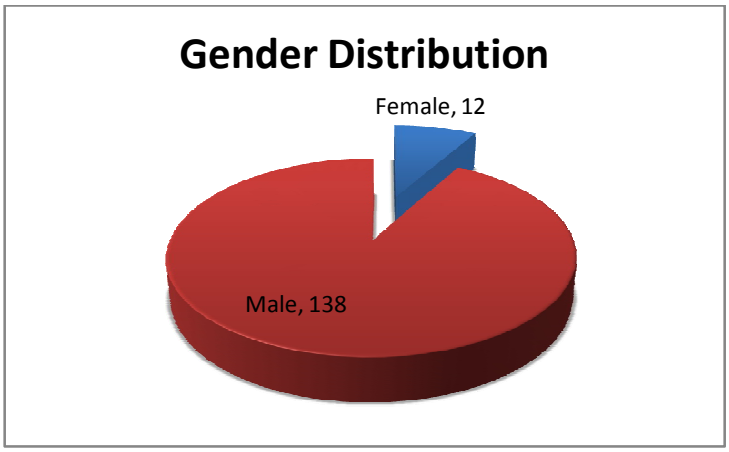
There was no significant difference between the two groups in the gender distribution. Among the 75 children in Group M, 70 were male and 5 were females whereas in Group T, 68 were males and 7 were females.

Crosstab for gender distribution

			DRUGGIVEN		Total
			Triclofos	Midazolam	
SEX	F	Number	7	5	12
		percentage	9.3%	6.7%	8.0%
	M	Number	68	70	138
		percentage	90.7%	93.3%	92.0%
Total		Number	75	75	150
		percentage	100.0%	100.0%	100.0%

Chi-Square Tests for gender distribution

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	.362	1	.547(not significant)		
Continuity Correction	.091	1	.763		
Likelihood Ratio	.364	1	.546		
Fisher's Exact Test				.765	.382
No of Valid Cases	150				



Frequency Table

SEX

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	12	8.0	8.0	8.0
	M	138	92.0	92.0	100.0

Cross tab for Age and Weight distribution:

	DRUG GIVEN	N	Mean	Std. Deviation	Std. Error Mean
AGE	Triclofos	75	4.2067	2.10483	.24304
	Midazolam	75	3.9400	2.12747	.24566
WEIGHT IN KG	Triclofos	75	13.85	3.283	.379
	Midazolam	75	13.68	3.116	.360

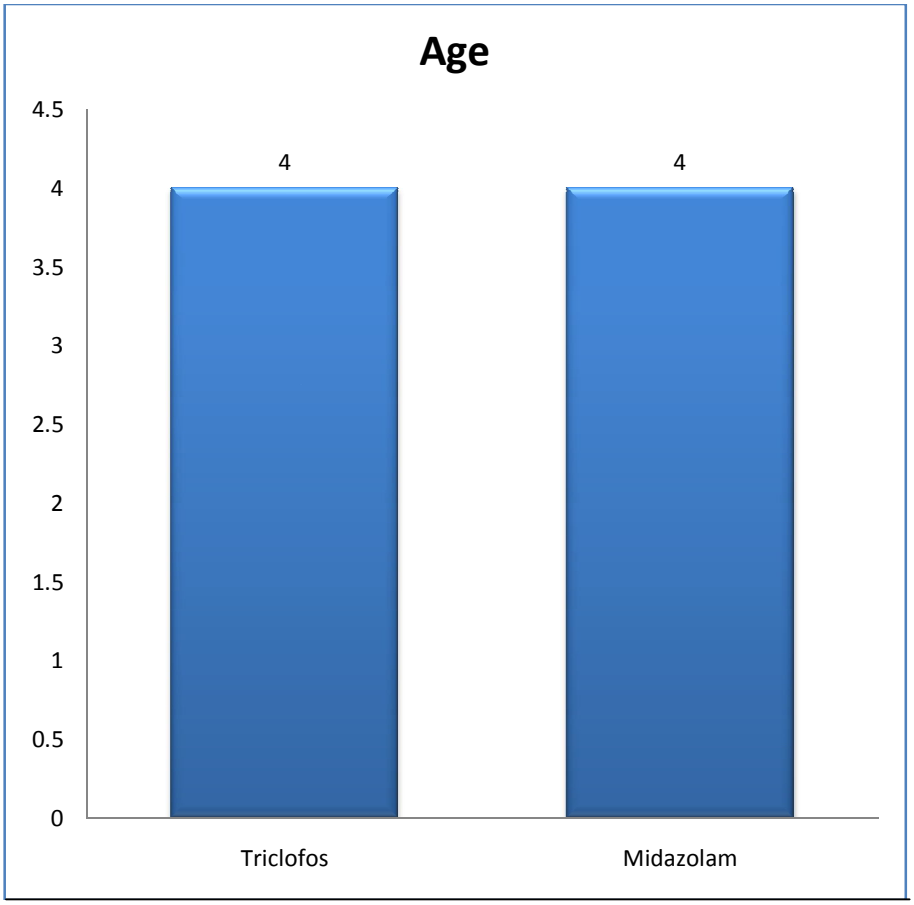
Independent Samples Test

		Levene's Test for Equality of Varianc	t-test for Equality of Means

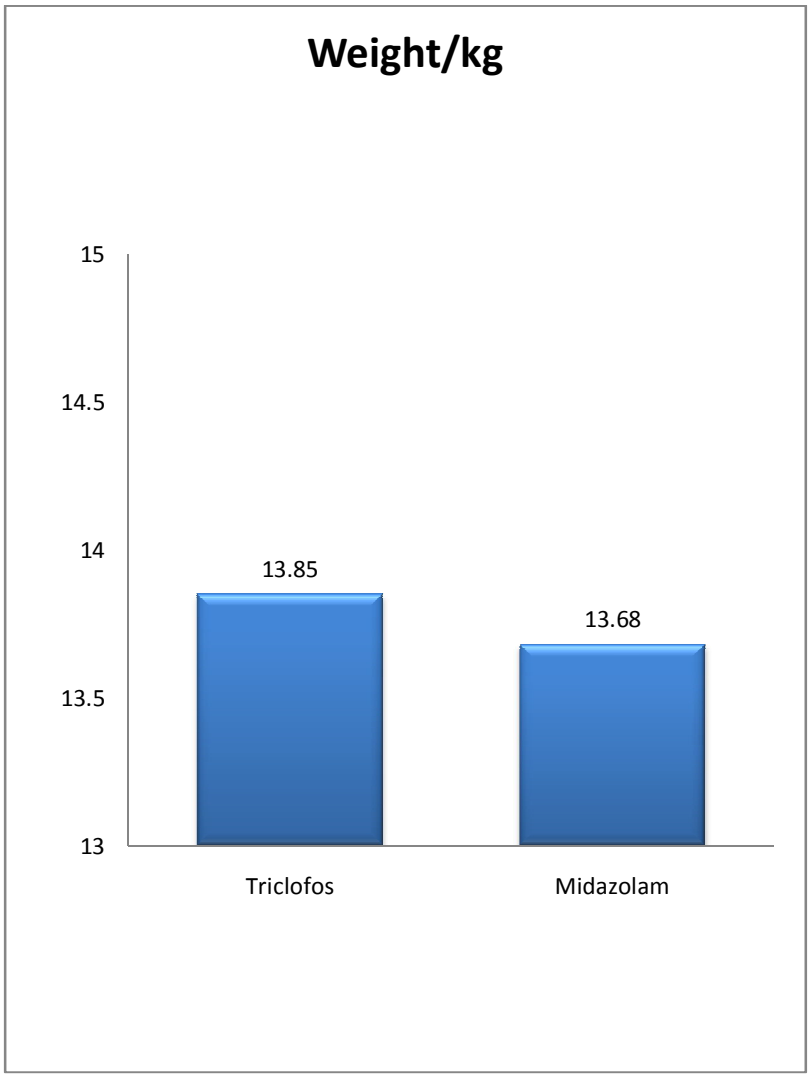
		es								
		F	Sig.	t	Df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
AGE	Equal variances assumes	.059	.808	.772	148	.442	.26667	.34557	-.41622	.94956
	Equal variances not assumed			.772	147.983	.442	.26667	.34557	-.41622	.94956
WEIGHT IN KG	Equal variances assumed	.712	.400	.332	148	.741	.173	.523	-.859	1.206
	Equal variances not assumed			.332	147.598	.741	.173	.523	-.859	1.206

There is no statistical significance (p>.05)
between the two groups in terms of age and weight of the patients.

Both groups were comparable in terms of age, the mean age being similar around 4 in both the groups.



In the weight distribution also, both the groups did not have any significant difference the mean weight being 13.7 kg



CROSSTAB FOR DIAGNOSIS

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	BALANOPOSTHITIS	1	.7	.7	.7
	ENCYSTED HYDROCELE OF CORD	1	.7	.7	1.3
	HYDROCELE	25	16.7	16.7	18.0
	INGUINAL HERNIA	14	9.3	9.3	27.3
	PENILE HYPOSPADIASIS	2	1.3	1.3	28.7
	PHIMOSIS	100	66.7	66.7	95.3
	POST PYELOLITHOTOMY	1	.7	.7	96.0
	PYELOPLASTY DONE	1	.7	.7	96.7
	UMBLICAL HERNIA	1	.7	.7	97.3
	UMBLICAL POLYP	1	.7	.7	98.0
	UNDESCENDED TESTIS	2	1.3	1.3	99.3
	VUJ CALCULUS	1	.7	.7	100.0
	Total	150	100.0	100.0	

CROSS TAB FOR PROCEDURE

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	ANATOMICAL REPAIR	1	.7	.7	.7
	CIRCUMCISION	101	67.3	67.3	68.0
	CYSTOSCOPY	1	.7	.7	68.7
	DJ STENT REMOVAL	2	1.3	1.3	70.0
	EXPLORATION	1	.7	.7	70.7
	HERNIOTOMY	15	10.0	10.0	80.7
	ORCHIDOPEXY	2	1.3	1.3	82.0
	PVSL	25	16.7	16.7	98.7
	URETHROPLASTY	2	1.3	1.3	100.0
	Total	150	100.0	100.0	

DRUG ACCEPTANCE SCORE FOR TRICLOFOS

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	50	66.7	66.7	66.7
	2	21	28.0	28.0	94.7
	3	4	5.3	5.3	100.0
	Total	75	100.0	100.0	

DRUG ACCEPTANCE SCORE FOR MIDAZOLAM

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	36	48.0	48.0	48.0
	2	35	46.7	46.7	94.7
	3	4	5.3	5.3	100.0
	Total	75	100.0	100.0	

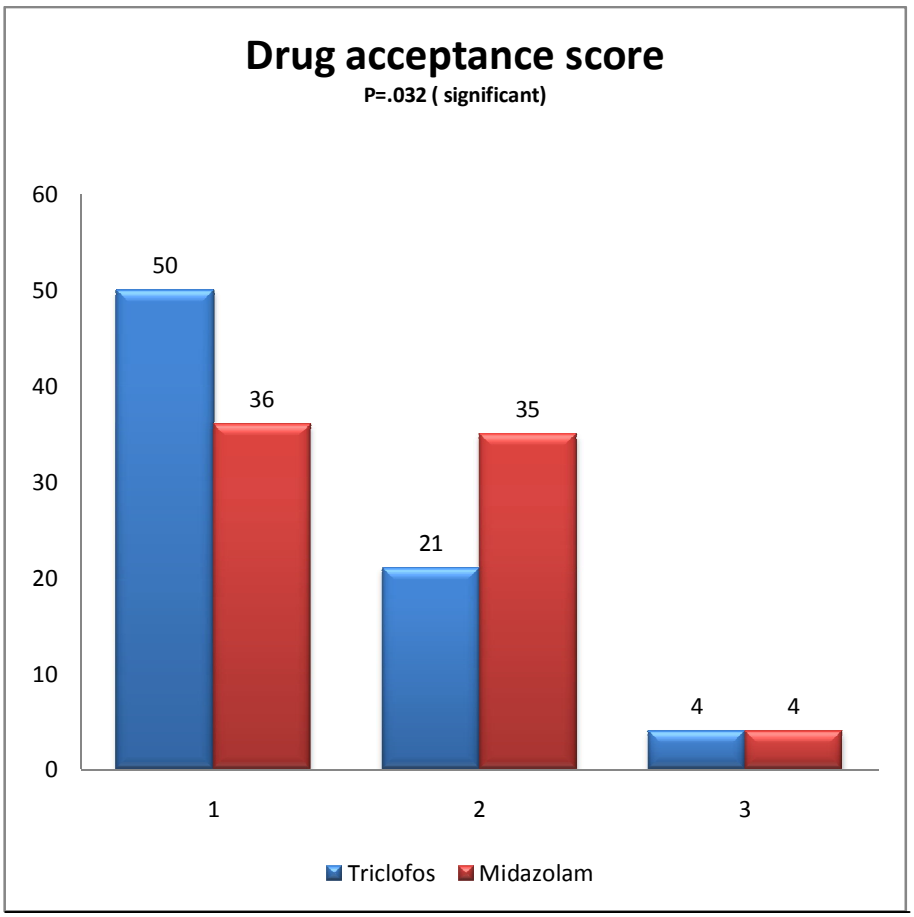
DRUG ACCEPTANCE SCORE

Ranks

	DRUG GIVEN	N	Mean Rank	Sum of Ranks
DRUG ACCEPTANCE SCORE	Triclofos	75	68.87	5165.50
	Midazolam	75	82.13	6159.50
	Total	150		

Test Statistics

	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig. (2-tailed)
DRUG ACCEPTANCE SCORE	2315.500	5165.500	-2.144	.032



Score 1=good-readily takes medicine

Score2=fair-accepts with persuasion

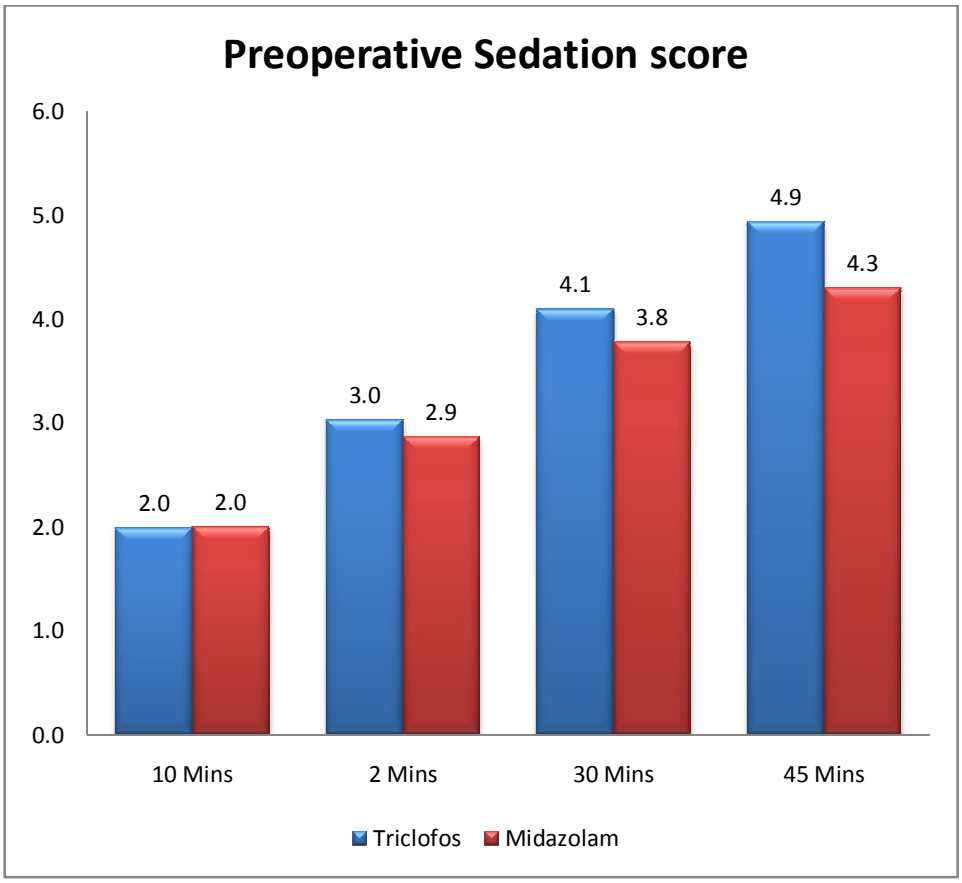
Score3=poor-unwilling to take medicine

Drug acceptance between the two groups showed a statistically significant

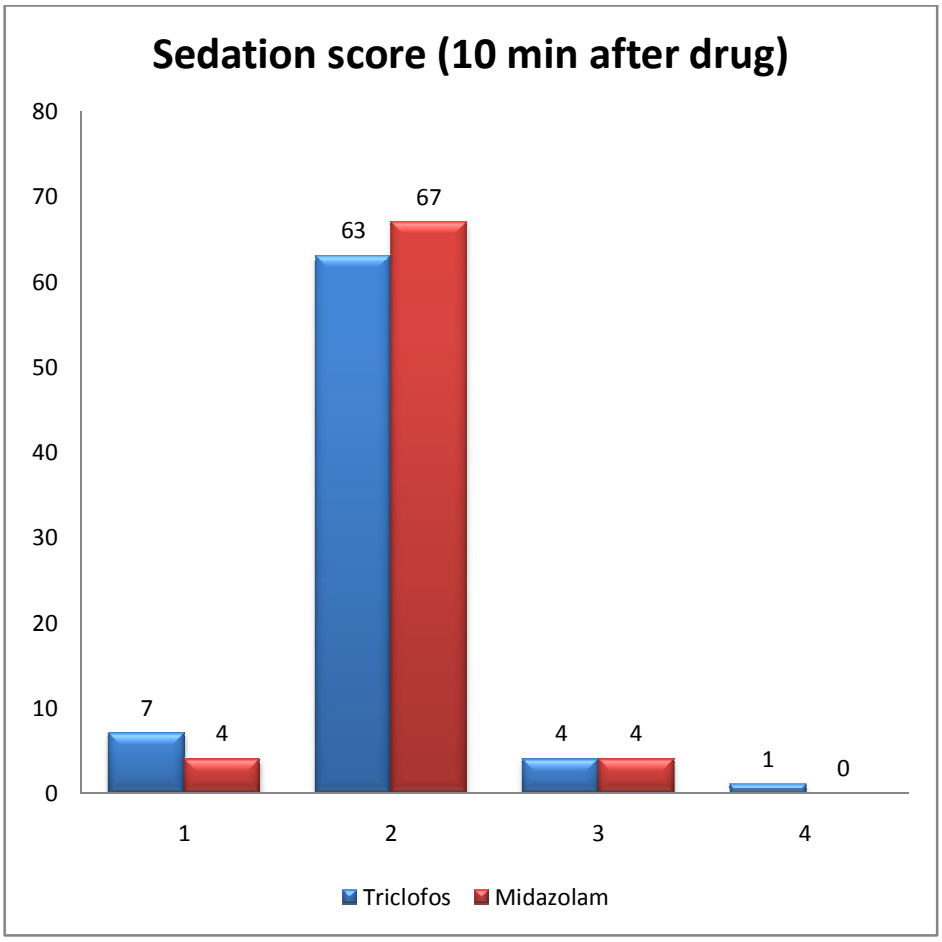
($p=0.032<0.05$) difference with triclofos better than midazolam.

The hemodynamic variables like the heart rate, respiratory rate and the oxygen saturation in the two groups were:

	DRUG GIVEN	N	Mean	Std. Deviation	Std. Error Mean
HR/MIN	Triclofos	75	110.97	18.698	2.159
	Midazolam	75	118.92	15.848	1.830
RR/MIN	Triclofos	75	21.44	3.523	.407
	Midazolam	75	22.24	3.377	.390
SpO2	Triclofos	75	98.33	.553	.064
	Midazolam	75	98.16	.521	.060



The sedation scores noted at various time intervals showed a significant difference between the midazolam and triclofos with triclofos better than the midazolam



There was no significant difference($p>0.05$) at 10 minutes of drug administration between the two drugs.

Crosstab for sedation score at 10 minutes after drug

			DRUGGIVEN		
			Triclofos	Midazolam	Total
Pre op Sedation Score 10MIN	1	number	7	4	11
		% within DRUGGIVEN	9.3%	5.3%	7.3%
	2	number	63	67	130
		% within DRUGGIVEN	84.0%	89.3%	86.7%
	3	number	4	4	8
		% within DRUGGIVEN	5.3%	5.3%	5.3%
	4	number	1	0	1
		% within DRUGGIVEN	1.3%	0.0%	.7%
Total		number	75	75	150
		% within DRUGGIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score at 10 min

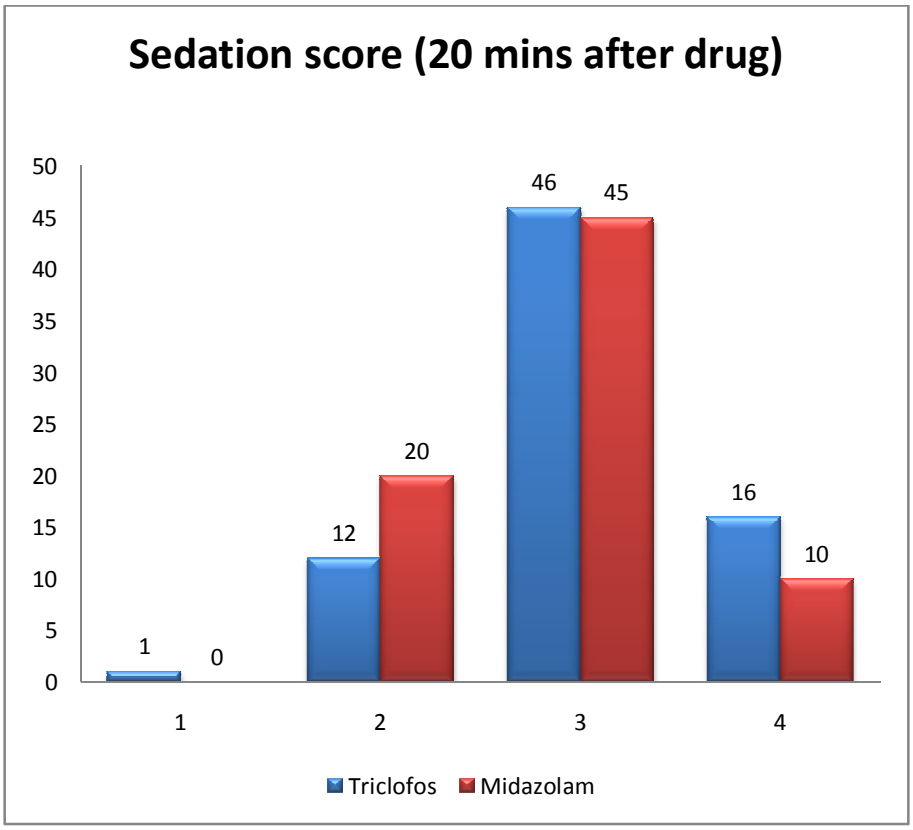
	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	1.941[a]	3	.585
Likelihood Ratio	2.338	3	.505
Linear-by-Linear Association	.043	1	.835
No of Valid Cases	150		

Crosstab for sedation score at 20 minutes after drug

			DRUGGIVEN		
			Triclofos	Midazolam	Total
Pre op SS 20MIN	1	number	1	0	1
		% within DRUG GIVEN	1.3%	0.0%	.7%
	2	number	12	20	32
		% within DRUG GIVEN	16.0%	26.7%	21.3%
	3	number	46	45	91
		% within DRUG GIVEN	61.3%	60.0%	60.7%
	4	number	16	10	26
		% within DRUG GIVEN	21.3%	13.3%	17.3%
Total		number	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 20 min after drug

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.396	3	.222
Likelihood Ratio	4.816	3	.186
Linear-by-Linear Association	2.323	1	.127
N of Valid Cases	150		



There was no significant difference ($p>0.05$) at 20 minutes after drug administration between both the drugs.

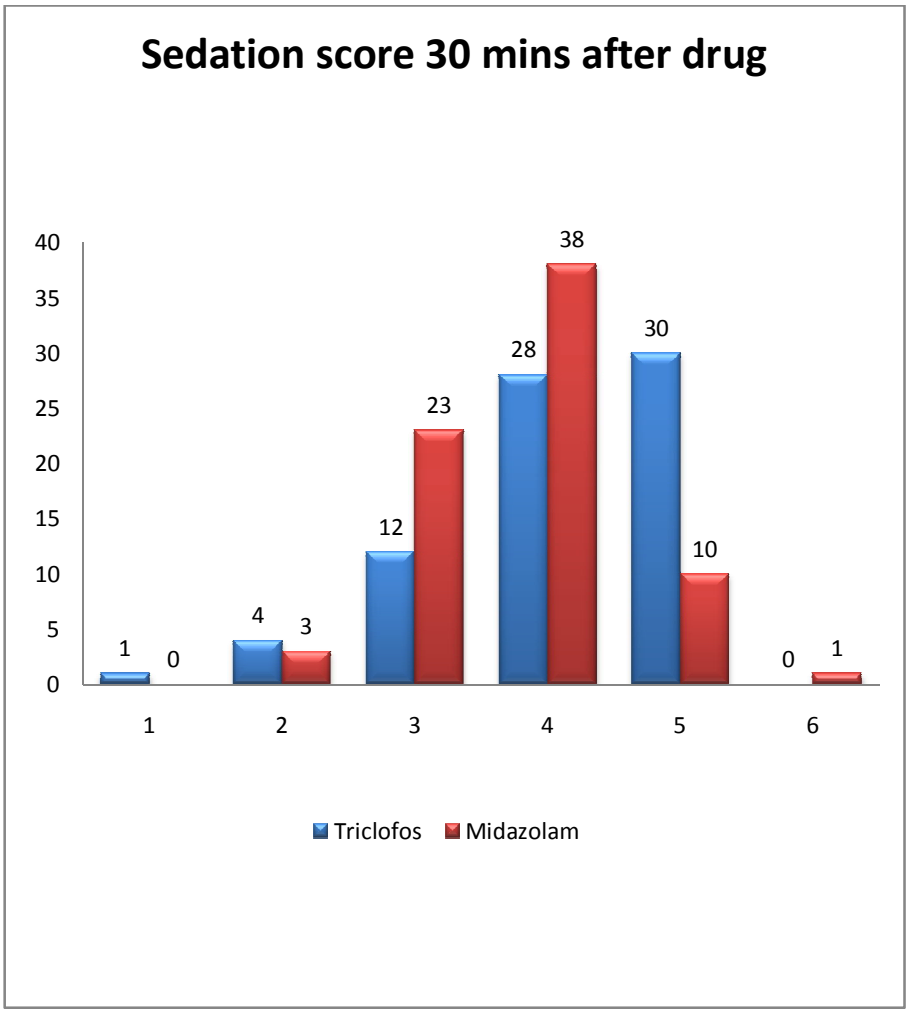
Crosstab for sedation score at 30 minutes of drug administration

			DRUGGIVEN		
			Triclofos	Midazolam	Total
Pre op SS 30MIN	1	Number	1	0	1
		% within DRUGGIVEN	1.3%	0.0%	.7%
	2	Number	4	3	7
		% within DRUGGIVEN	5.3%	4.0%	4.7%
	3	Number	12	23	35
		% within DRUGGIVEN	16.0%	30.7%	23.3%
	4	Number	28	38	66
		% within DRUGGIVEN	37.3%	50.7%	44.0%
	5	Number	30	10	40
		% within DRUGGIVEN	40.0%	13.3%	26.7%
	6	Number	0	1	1
		% within DRUGGIVEN	0.0%	1.3%	.7%
Total		Number	75	75	150
		% within DRUGGIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 30 min after drug

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	17.115[a]	5	.004
Likelihood Ratio	18.418	5	.002
Linear-by-Linear Association	4.961	1	.026
No of Valid Cases	150		

There was a significant difference ($p<0.05$) between the two groups at 30 minutes of drug administration where 40% of the children in the triclofos group were in score 5 (asleep, sluggish response to stimulus) whereas in midazolam group it is only 13.3%.

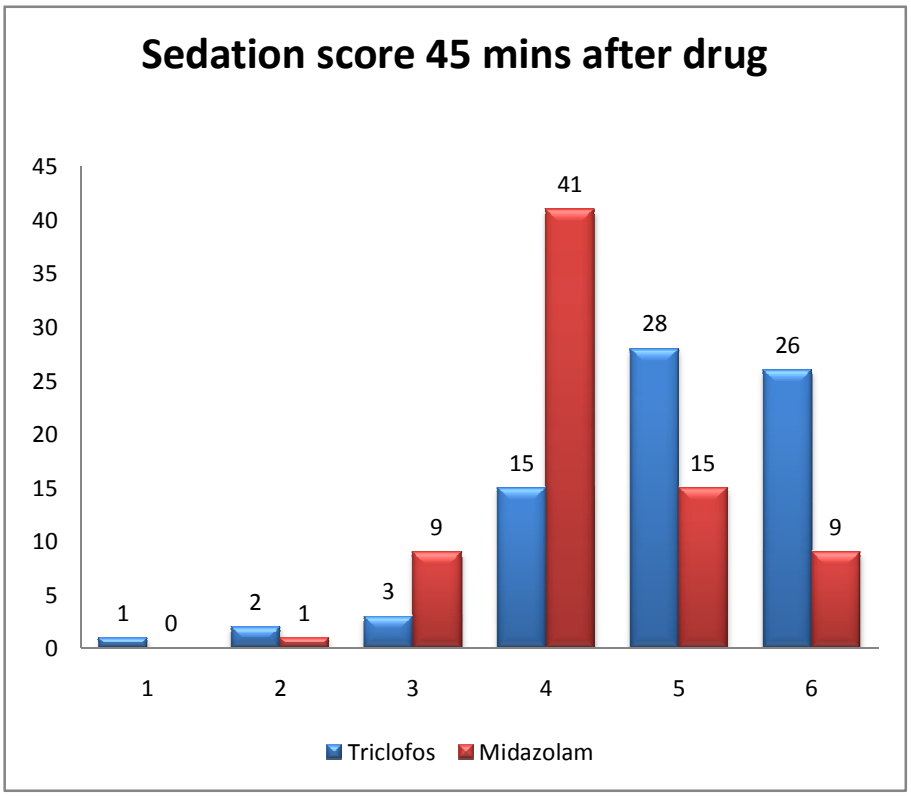

Sedation score 30 mins after drug
40
35
30
25
20
15
10
5
0
1
0
4
3
12
23
28
38
30
10
0
1
1
2
3
4
5
6
Triclofos
Midazolam

Crosstab for sedation score after 45 minutes of drug

			DRUGGIVEN		
			Triclofos	Midazolam	Total
Pre op SS 45MIN	1	Number	1	0	1
		% within DRUGGIVEN	1.3%	0.0%	.7%
	2	Number	2	1	3
		% within DRUGGIVEN	2.7%	1.3%	2.0%
	3	Number	3	9	12
		% within DRUGGIVEN	4.0%	12.0%	8.0%
	4	Number	15	41	56
		% within DRUGGIVEN	20.0%	54.7%	37.3%
	5	Number	28	15	43
		% within DRUGGIVEN	37.3%	20.0%	28.7%
	6	Number	26	9	35
		% within DRUGGIVEN	34.7%	12.0%	23.3%
Total		Number	75	75	150
		% within DRUGGIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 45 min after drug

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	28.592[a]	5	.000
Likelihood Ratio	30.022	5	.000
Linear-by-Linear Association	14.342	1	.000
No of Valid Cases	150		



There was significant difference between the two groups(p=.000<.05), when sedation score at 45 minutes after drug administration was considered, with triclofos being better than midazolam as 34% of children in triclofos groupwere in score 6(no response to firm nail bed pressure or other noxious stimuli) compared to 12% of them in the midazolam group.

Test Statistics

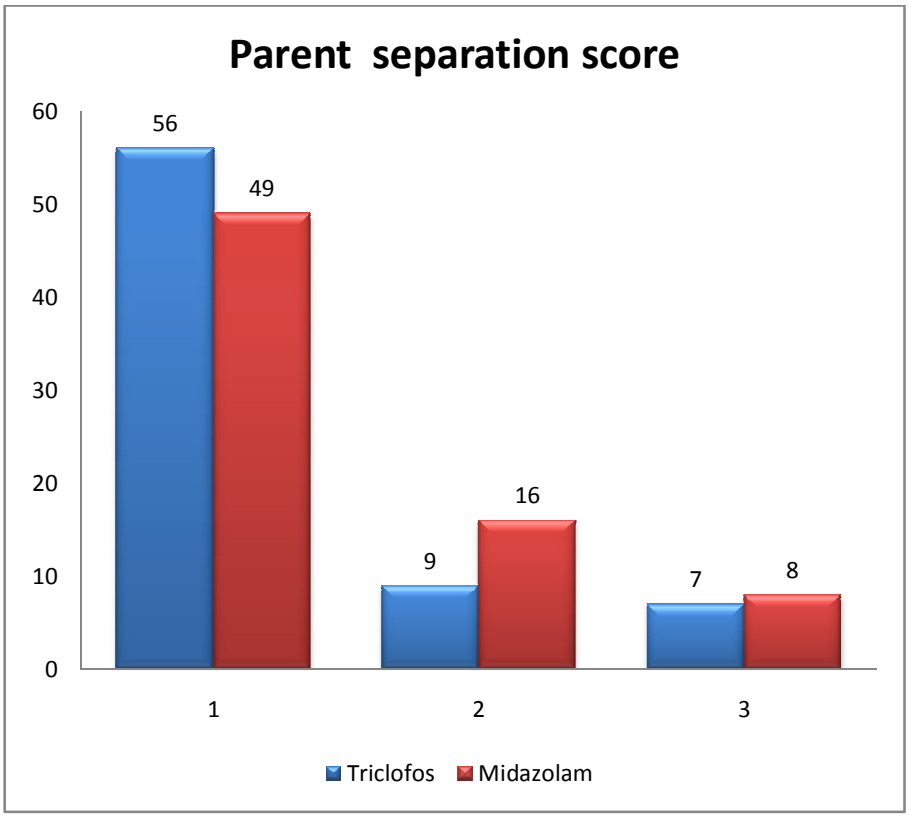
	Mann-Whitney U	Wilcoxon W	Z	Asymp. Sig. (2-tailed)
Pre op SS10MIN	2743.500	5593.500	-.439	.585
Pre op SS20MIN	2430.000	5280.000	-1.647	.222
Pre op SS30MIN	2115.000	4965.000	-2.790	.004
Pre op SS45MIN	1679.000	4529.000	-4.463	.000
PARENT SEPARATION SCORE	2590.000	5440.000	-1.036	.300
MASK ACCEPTANCE SCORE	1616.500	4466.500	-4.924	.000

PARENT SEPARATION SCORE FOR TRICLOFOS GROUP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	56	74.7	74.7	74.7
	2	9	12.0	12.0	86.7
	3	7	9.3	9.3	96.0
	4	3	4.0	4.0	100.0
	Total	75	100.0	100.0	

PARENT SEPARATION SCORE FOR MIDAZOLAM GROUP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	49	65.3	65.3	65.3
	2	16	21.3	21.3	86.7
	3	8	10.7	10.7	97.3
	4	2	2.7	2.7	100.0
	Total	75	100.0	100.0	



Score 1-calm and sleepy

Score 2-apprehensive but withdrawn from surroundings

Score 3-crying

There was no significant difference between the two groups ($p=0.3>0.05$) as seen from the above tables, in the parent separation score.

MASK ACCEPTANCE SCORE FOR TRICLOFOS

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	5	6.7	6.7	6.7
	2	2	2.7	2.7	9.3
	3	13	17.3	17.3	26.7
	4	55	73.3	73.3	100.0
	Total	75	100.0	100.0	

MASK ACCEPTANCE SCORE FOR MIDAZOLAM

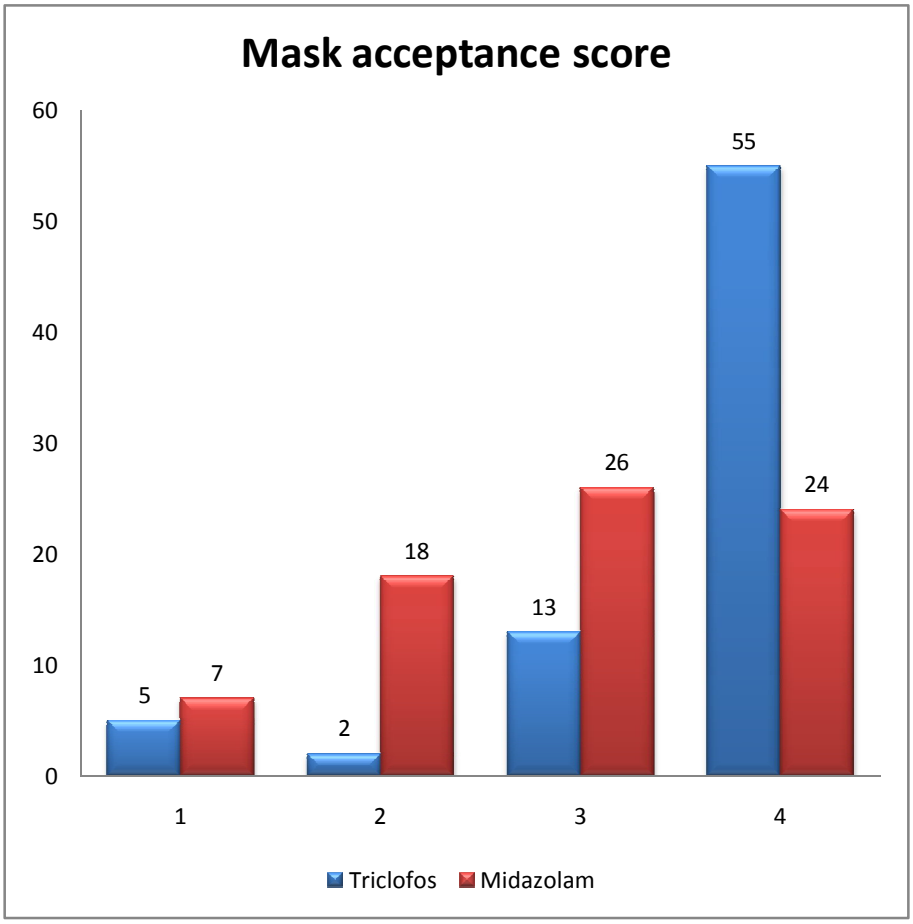
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	7	9.3	9.3	9.3
	2	18	24.0	24.0	33.3
	3	26	34.7	34.7	68.0
	4	24	32.0	32.0	100.0
	Total	75	100.0	100.0	

1-Poor-afraid,combative,crying

2-Fair-moderate fear of mask, not easily calmed

3-Good-slight fear of mask, easily calmed

4-Excellent- unafraid,cooperative,accepts mask easily



There was a significant difference between the two drugs($p=0.00<0.05$), in terms of mask acceptance score with triclofos having excellent mask acceptance as depicted above. 73% of children in triclofos group have score 4(unafraid, cooperative, accepts mask easily) whereas only 32% of the children in midazolam group have score 4.

Paired Samples Statistics for triclofos

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Preop HR	110.97	75	18.698	2.159
	Intraop HR	111.68	75	16.789	1.939
Pair 2	Preop RR	21.44	75	3.523	.407
	Intraop RR	22.27	75	9.599	1.108
Pair 3	Pre op SpO2	98.33	75	.553	.064
	Intraop SpO2	98.24	75	.541	.063

Paired Samples Test for triclofos

		Paired Differences					t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Preop HR – Intra op HR	-.707	15.366	1.774	-4.242	2.829	-.398	74	.692
Pair 2	Preop RR – Intraop RR	-.827	10.491	1.211	-3.240	1.587	-.682	74	.497
Pair 3	PreopSpO2 - IntraopSpO2	.093	.720	.083	-.072	.259	1.123	74	.265

As evident from the above statistical analysis, there is no significant variation of heart rate, respiratory rate and oxygen saturation intra operatively after triclofos administration.

Paired Samples Statistics for midazolam

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Preop HR	118.92	75	15.848	1.830
	Intraop HR	119.17	75	16.122	1.862
Pair 2	Preop RR	22.24	75	3.377	.390
	Intraop RR	21.67	75	2.844	.328
Pair 3	Preop SpO2	98.16	75	.521	.060
	Intraop SpO2	98.05	75	.399	.046

Paired Samples Test for midazolam

		Paired Differences					T	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Preop HR – Intraop HR	-.253	10.743	1.240	-2.725	2.218	-.204	74	.839
Pair 2	Preop RR – Intraop RR	.573	3.313	.383	-.189	1.336	1.499	74	.138
Pair 3	Preop SpO2 – Intraop SpO2	.107	.559	.065	-.022	.235	1.652	74	.103

The above statistical analysis depicts that there is no significant variation of heart rate, respiratory rate and oxygen saturation intra operatively after midazolam administration.

Crosstab for postop sedation score at 1 hour

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST OP SEDATION SCORE at 1HOUR	1	number	2	0	2
		% within DRUGGIVEN	2.7%	0.0%	1.3%
	2	number	3	2	5
		% within DRUGGIVEN	4.0%	2.7%	3.3%
	3	number	5	15	20
		% within DRUGGIVEN	6.7%	20.0%	13.3%
	4	number	45	46	91
		% within DRUGGIVEN	60.0%	61.3%	60.7%
	5	number	20	11	31
		% within DRUGGIVEN	26.7%	14.7%	20.7%
	6	number	0	1	1
		% within DRUGGIVEN	0.0%	1.3%	.7%
Total		number	75	75	150
		% within DRUGGIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 1 hour after surgery

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	10.824	5	.055
Likelihood Ratio	12.255	5	.031
Linear-by-Linear Association	.866	1	.352
No of Valid Cases	150		

There was no significant difference in the post operative sedation score at 1 hour between both the drugs(p=.055>0.05)

Crosstab for sedation score 2hrs postop

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST OP SEDATION SCORE AT 2HRS	1	NUMBER	3	0	3
		% within DRUG GIVEN	4.0%	0.0%	2.0%
	2	NUMBER	4	7	11
		% within DRUG GIVEN	5.3%	9.3%	7.3%
	3	NUMBER	33	46	79
		% within DRUG GIVEN	44.0%	61.3%	52.7%
	4	NUMBER	33	17	50
		% within DRUG GIVEN	44.0%	22.7%	33.3%
	5	NUMBER	2	5	7
		% within DRUG GIVEN	2.7%	6.7%	4.7%
Total		NUMBER	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 2 hours after surgery

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	12.363[a]	4	.015
Likelihood Ratio	13.676	4	.008
Linear-by-Linear Association	.564	1	.453
No of Valid Cases	150		

There was significant difference between the two groups at 2 hours post op(p.015<0.05),with larger number of children still in higher levels of sedation in midazolam group compared to triclofos group.

Crosstab for postop sedation at 3 hrs

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST OP SEDATION SCORE 3HRS	1	NUMBER	3	1	4
		% within DRUG GIVEN	4.0%	1.3%	2.7%
	2	NUMBER	16	19	35
		% within DRUG GIVEN	21.3%	25.3%	23.3%
	3	NUMBER	43	45	88
		% within DRUG GIVEN	57.3%	60.0%	58.7%
	4	NUMBER	13	9	22
		% within DRUG GIVEN	17.3%	12.0%	14.7%
	5	NUMBER	0	1	1
		% within DRUG GIVEN	0.0%	1.3%	.7%
Total		NUMBER	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 3 hours after surgery

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	3.030	4	.553
Likelihood Ratio	3.467	4	.483
Linear-by-Linear Association	.013	1	.908
N of Valid Cases	150		

There was no significant difference between the two groups ($p>0.05$) in terms of postop sedation score at 3 hours.

Crosstab for post op sedation score at 4 hours

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST OP SEDATION SCORE AT 4HRS	1	NUMBER	7	4	11
		% within DRUGGIVEN	9.3%	5.3%	7.3%
	2	NUMBER	27	39	66
		% within DRUGGIVEN	36.0%	52.0%	44.0%
	3	NUMBER	40	28	68
		% within DRUGGIVEN	53.3%	37.3%	45.3%

	4	NUMBER	1	3	4
		% within DRUGGIVEN	1.3%	4.0%	2.7%
	5	NUMBER	0	1	1
		% within DRUGGIVEN	0.0%	1.3%	.7%
Total		NUMBER	75	75	150
		% within DRUGGIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 4 hours after surgery

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	7.118	4	.130
Likelihood Ratio	7.584	4	.108
Linear-by-Linear Association	.054	1	.816
No of Valid Cases	150		

As seen from the above table there is no significant difference (p=0.13>0.05) noted between the two groups for postop sedation score at 4hrs.

Crosstab for sedation score at 5hrs postop

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST SEDATION SCORE AT 5HRS	1	NUMBER	8	5	13
		% within DRUG GIVEN	10.7%	6.7%	8.7%
	2	NUMBER	42	54	96
		% within DRUG GIVEN	56.0%	72.0%	64.0%
	3	NUMBER	25	14	39
		% within DRUG GIVEN	33.3%	18.7%	26.0%
	4	NUMBER	0	2	2
		% within DRUG GIVEN	0.0%	2.7%	1.3%
Total		NUMBER	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score 5 hours after surgery

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	7.295[a]	3	.063
Likelihood Ratio	8.120	3	.044
Linear-by-Linear Association	.294	1	.587
No of Valid Cases	150		

No significant difference was noted between the groups($p=0.063>0.05$), when considering the postop sedation score at 5 hours.

Crosstab for sedation score 6 hrs postop

			DRUGGIVEN		
			Triclofos	Midazolam	Total
POST OP SEDATION SCORE 6HRS	1	NUMBER	8	16	24
		% within DRUG GIVEN	10.7%	21.3%	16.0%
	2	NUMBER	63	54	117
		% within DRUG GIVEN	84.0%	72.0%	78.0%
	3	NUMBER	4	4	8
		% within DRUG GIVEN	5.3%	5.3%	5.3%
	4	NUMBER	0	1	1
		% within DRUG GIVEN	0.0%	1.3%	.7%
Total		NUMBER	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for sedation score

6hrs after surgery

	Value	Df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.359[a]	3	.225
Likelihood Ratio	4.798	3	.187
Linear-by-Linear Association	1.031	1	.310
No of Valid Cases	150		

No significant difference(p=0.225>0.05) in postop sedation score at 6 hrs between the two groups

FREQUENCY TABLE FOR ADVERSE EFFECTS

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	LARYNGOSPASM	2	1.3	1.3	4.0
	NIL	140	93.3	93.3	97.3
	RESPIRATORY DEPRESSION	1	.7	.7	98.0
	SHIVERING	1	.7	.7	98.7
	VOMITING	2	1.3	1.3	100.0
	Total	150	100.0	100.0	

Crosstab for adverse effects

			DRUGGIVEN		
			Triclofos	Midazolam	Total
ADVERSE EFFECTS	LARYNGOSPASM	NUMBER	0	2	2
		% within DRUG GIVEN	0.0%	2.7%	1.3%
	NIL	NUMBER	71	69	140
		% within DRUG GIVEN	94.7%	92.0%	93.3%
	RESPIRATORY DEPRESSION	NUMBER	1	0	1
		% within DRUG GIVEN	1.3%	0.0%	.7%
	SHIVERING	NUMBER	1	0	1
		% within DRUG GIVEN	1.3%	0.0%	.7%
	VOMITING	NUMBER	1	1	2
		% within DRUG GIVEN	1.3%	1.3%	1.3%
Total		NUMBER	75	75	150
		% within DRUG GIVEN	100.0%	100.0%	100.0%

Chi-Square Tests for adverse effects

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	5.029	5	.412
Likelihood Ratio	6.620	5	.250
No of Valid Cases	150		

No significant difference in the occurrence of adverse effects in the two groups as evident from p value=0.412>0.05.(not significant).

ANALYSIS OF STATISTICAL DATA:

S.NO	PARAMETER ASSESSED	P VALUE	SIGNIFICANT OR NOT
1	Age	0.442	No
2	Gender	0.547	No
3	Weight	0.741	No
4	**Drug acceptance score**	**0.032**	**Yes**
5	Sedation score at 10 min	0.585	No
6	Sedation score at 20 min	0.222	No
7	**Sedation score at 30 min**	**0.004**	**Yes**
8	**Sedation score at 45 min**	**0.000**	**Yes**
9	Parent separation score	0.300	No
10	**Mask acceptance score**	**0.000**	**Yes**
11	Postop sedation score at 1hr	0.055	No
12	**Postop sedation score at 2hrs**	**0.015**	**Yes**
13	Postop sedation score at 3hrs	0.553	No
14	Postop sedation score at 4hrs	0.130	No
15	Postop sedation score at 5hrs	0.063	No
16	Adverse effects	0.412	No

DISCUSSION:

Premedication in children is necessary to allay fear and anxiety before surgery and provide a smoother anaesthesia for the children. The search for a perfect premedicant has been on and continues. So we have done this study to find out a good premedication out of the ones widely used.We have chosen to compare oral midazolam and triclofos which is being used as sedative for short procedures.

The sample size of 142 was arrived with G* power 3.13 version with reference to parent study, and 150 cases was taken into study accounting for any dropout from the study due to practical difficulties like spitting out of the drug, etc.

ASA PS 1 cases were chosen so that there are no major side effects by the drug or by the co existing diseases. The maximum weight allowed in the study was 20 kg to avoid giving large volume of drug as premedication. Luz Maria et al[12], have accepted ASA 1 and 2 patients for their study on evaluating the efficacy of oral midazolam with acetaminophen for premedication. Wilson et al[16], selected ASA 1 patients for their study on the effectiveness of oral midazolam for sedation in orthodontic procedures.

The dose of the drug was chosen as Midazolam 0.5mg/kg based on the study Premedication of children with midazolam by Mc Millan, et al[32] which concluded that oral midazolam given at a dose of 0.5 mg/kg was effective at causing sedation without any side effects. Fazi et al[25], in a study to compare oral midazolam and clonidine for sedation of paediatric tonsillectomy patients used midazolam as 0.5 mg/kg. Shabbir et al[8], in their study for comparison of conscious sedation between oral midazolam and triclofos used midazolam 0.5 mg/kg orally

The dose of triclofos was 75mg/kg based on the studies of Aruna Parameswari et al[2] and Sujata Chaudhary et al[1], where the dose of 75 mg/kg proved effective in both the studies. R.K.Gupta et al[18], in their study on oral premedication in children had used oral triclofos in the dose of 75mg/kg. Bhatnagar et al[20], in their study on comparison of oral midazolam with oral tramadol, triclofos and zolpidem for sedation of paediatric dental patients used triclofos in the dose of 70mg/kg.

The usage of intravenous preparation of midazolam given orally mixed with a vehicle in our study to make it palatable and the fact that it is more reliable and effective than the commercially available oral formulation is supported by the study of Brosius KK et al[26] ,where the study proved that the iv preparation mixed with a vehicle produced a

more reliable sedation and higher plasma level of the drug compared to the equivalent dose of the commercially available preparation. The drugs were given 45 minutes prior to induction time to match the peak effect of both the drugs in common[2].

The age distribution was comparable in our study, with the mean age being 4 years in both the groups and insignificant difference was noted(p=0.442) between the two groups. The gender difference between the midazolam and triclofos group was not significant (p=0.547) and the weight in kilograms of the children in both the groups was on an average 13.7 kg without any significant difference (p=0.741). This is in favour that any difference between the two groups in demographic profiles would be purely by chance.

The aim of our study was to compare the sedative effects of oral midazolam and oral triclofos. Triclofos was better in our study as a good sedative, with the sedation score significantly better(p=0.000) with triclofos than midazolam which is in concordance with Aruna Prameswari et al study where they concluded triclofos as a better sedative and anxiolytic than midazolam.

The drug acceptance was better with triclofos shown by a statistically significant difference(p=0.032) in contrary to the study by

Sujata Chaudhary et al[1] in which greater percentage of children were complaint with midazolam than triclofos but with a statistically insignificant difference. Aruna Parameswari et al[2], in the study for comparison of sedative effects of triclofos and midazolam had 80% of the patients in midazolam group accepted the drug whereas 20% resisted the drug, but in triclofos group 75% accepted the drug and 25% resisted the drug but the difference between the two groups was not statistically significant.

The difference in preoperative sedation scores at 10 minutes($p=0.585$) of drug administration was not significant. Of the 75 children in the triclofos group, 63 were in the score 2(patient awake,cooperative, oriented and tranquil) and 67 out of 75 in midazolam group were in score 2.

Sedation score at 20 minutes of drug administration showed no significant difference ($p=0.222$) between the two drugs.In triclofos group 46 children were in score 3(patient drowsy, with response to commands) and 45 children in midazolam group were in score 3.

Whereas the sedation scores at 30 minutes of drug intake showed 30 children (40%) in score 5(patient asleep, sluggish response to stimulus) in triclofos group, but the midazolam group had only 10

children(13%) in score 5 , which means there is a statistically significant difference(0.004).

The preoperative sedation score showed a highly significant difference (p=0.000) at 45 minutes of drug administration with the triclofos group having 34% of the children in score 6(no response to firm nail bed pressure or other noxious stimuli) against midazolam group which had only 12% of children in score 6.

So it was evident from the preoperative sedation scores , that triclofos produces better sedation than midazolam which is similar to the results of the study of Aruna Parameswari et al[2], where only 5% of patients in midazolam group after 30 minutes were asleep as compared to 65% sedated patients after 90 minutes in the triclofos group, showing a significant difference. Bhatnagar et al[20], in comparing oral midazolam with triclofos and two other drugs , triclofos had better sedation score when compared to midazolam.

Mohamed et al[9] , found that oral midazolam with ketamine provided high sedation levels after 30 minutes of administration when compared to dexmedetomidine in their study. Wilson et al[16] in studying the effectiveness of oral midazolam sedation for paediatric orthodontic procedures, found that the mean level of sedation to be greater for

midazolam when compared to nitrous oxide. Singh et al[24], found midazolam to be the best sedative among the three drugs(midazolam, triclofos, promethazine) for conscious sedation in paediatric dentistry.

The parent separation score was comparable between the two groups in the present study(p=0.3).Sujata Chaudhary et al[1], in their study also showed comparable parent separation score with both midazolam and triclofos. Luz Maria et al[12], in their study on efficacy of oral midazolam combined with acetaminophen showed that 86% of children were quiet at parent separation.

The mask acceptance score was good with triclofos as compared to midazolam (p=0.00) in our study. In contrary, Aruna parameswari, et al[2], have depicted a better mask acceptance with midazolam in their study comparing 40 children with 20 in each group. Whereas Sujata Chaudhary et al[1], had no difference in both the groups when comparing 20 children in the midazolam group with 20 in the triclofos group for mask acceptance. Nicole Almanrader et al[7] , found no statistical difference between clonidine and midazolam for mask acceptance with 86% satisfactory mask induction in midazolam group and 83% in clonidine group. Mohamed et al[9], study demonstrated better facemask acceptance at

induction in the midazolam ketamine group when compared to dexmedetomidine group.

The postoperative sedation scores at 2 hours postoperative showed significant difference between the triclofos and midazolam (p=0.015), with midazolam showing greater percentage of the children in higher sedation levels but the post operative sedation scores at 1hour, 3 hours, 4 hours , 5 hours and 6 hours showed no significant difference between the two groups. Sujata Chaudhary et al[1], found no significant difference in the post operative recovery characteristics in the midazolam and triclofos group in their study. There was no significant difference in the recovery profile between the butorphanol and midazolam group in the study by Sinha et al[13]. No significant difference noted by Saarnivaara et al[17] in the recovery scores between chloral hydrate and midazolam in children .

The hemodynamic variables in the two groups were mean heart rate 110.97(±18.6) in the triclofos group and 118.92(±15.8) in the midazolam group , mean respiratory rate was 21.44(±3.52) in triclofos group and 22.24(±3.37), mean oxygen saturation was 98.33(±0.553) in triclofos group and 98.16(±0.521) .The intraoperative hemodynamics did not show a significant variation from the preoperative values in both the groups (p>0.05) There was no significant variation of heart

rate(p=0.692), respiratory rate(p=0.497) and oxygen saturation(p=0.265) intra operatively after triclofos administration and also no significant variation of heart rate(p=0.839), respiratory rate(p=0.138) and oxygen saturation(p=0.103) intra operatively after midazolam administration. Sujata Chaudhary et al[1] have shown decrease in heart rate and blood pressure in both the triclofos and midazolam groups after drug administration.

The adverse effects occurred were minimal and were statistically insignificant(p=0.412). Laryngospasm occurred in 2 children in the midazolam , treated with 100% O2 ; vomiting occurred in 1child in each group, Inj. Ondansetron given iv. One child in triclofos group had shivering.

LIMITATIONS:

The peak onset of action of the two drugs are not similar but the difference is only 10-15 minutes. As the study included only day care surgery, most of the children were males presenting with phimosis, hernia and hydrocele for surgery. The volume of drug in both the groups could not be kept constant as drug was administered on weight basis and the two drugs are available as different per millilitre doses.

Summary:

Demographic profiles were comparable between the two groups. Triclofos being more palatable, was better accepted by the children, produced excellent sedation after 45 minutes of drug administration than midazolam. The parent separation score was comparable between the two groups. The mask acceptance score was good with triclofos than midazolam. The postoperative recovery score was better with triclofos.

Conclusion:

Based on our study " Randomised clinical trial to compare the sedative effects of oral triclofos with oral midazolam as premedicants in children", we find Triclofos is a better and safe sedative than midazolam given as premedicant in paediatric patients.

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PROFORMA:

NAME: AGE/SEX: IP

NO.:

DATE: Wt.:

GROUP:

DIAGNOSIS:

SURGERY:

BRIEF HISTORY:

COEXISTING ILLNESS:

EXAMINATION:

PR: CVS:

BP: RS:

RR:

INVESTIGATIONS:

Hb: BLOOD UREA:

URINE ALB: SUGAR:

SUGAR: Sr. CREATININE:

ANESTHESIA DETAILS:

PREMEDICATION:

INDUCTION

MAINTENANCE

PARAMETERS OBSERVED

PRE OP SEDATION SCORE

10 min	20 min	30 min	40 min	45 min

DRUG COMPLIANCE SCORE	SEDATION SCORE AT 45 MIN	PARENT SEPARATION SCORE	MASK ACCEPTANCE SCORE	MEAN HR	MEAN SpO2	MEAN RR

Hemodynamic parameters during surgery and post op:

	5 min	10 min	15 min	20min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min
HR												
RR												
SpO2												

POST OP SEDATION SCORE

1 Hr	2 Hr	3 Hr	4 Hr	5 Hr	6 Hr